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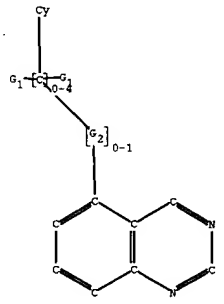
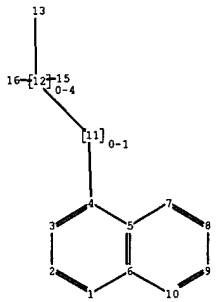




chain nodes :
11 12 13 15 16
ring nodes :
1 2 3 4 5 6 7 8 9 10
chain bonds :
4-11 11-12 12-13 12-15 12-16
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10
exact/norm bonds :
4-11 11-12 12-13 12-15 12-16
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10

G1:H,Ak

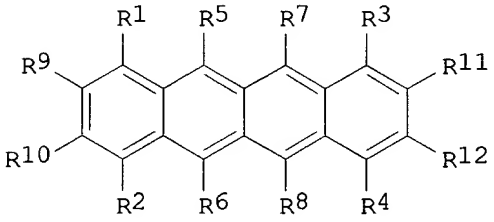
G2:O,S,N

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom
10:Atom 11:CLASS 12:CLASS 13:Atom 15:CLASS 16:CLASS
Generic attributes :
13:
Saturation : Unsaturated

L14 ANSWER 1 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 2002:247051 CAPLUS
DN 136:286307
TI Naphthacene derivatives, organic electroluminescent devices and materials using them
IN Kanno, Masaki; Suda, Yasumasa; Onikubo, Shunichi
PA Toyo Ink Mfg. Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 39 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

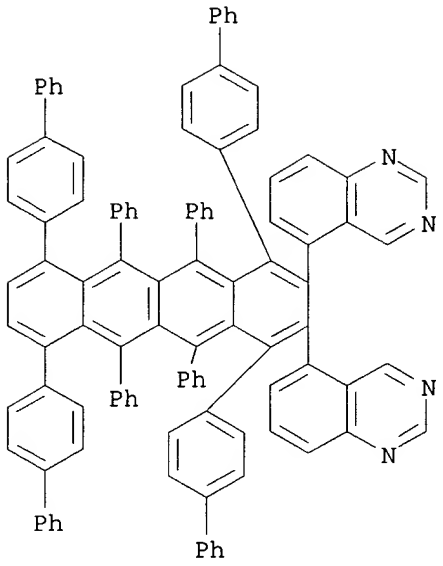
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002097465	A2	20020402	JP 2000-289680	20000925

OS MARPAT 136:286307
GI



I

AB The invention relates to an org. electroluminescent device comprising a general formula I [R1-12 = H, halo, or (un)substituted org. residue groups selected from alkyl, aryl, alkoxy, aryloxy, alkylthio, arylthio, amino and heterocyclyl; adjacent substituents of R1-12 may form a ring; .gtoreq.7 R1-12 are (un)substituted aryl; R1-4 can not be H simultaneously].
IT **405881-83-6P**
RL: DEV (Device component use); SPN (Synthetic preparation); PREP (Preparation); USES (Uses)
(naphthacene derivs., org. electroluminescent devices and materials using them)
RN 405881-83-6 CAPLUS
CN Quinazoline, 5,5'-[1,4,7,10-tetrakis([1,1'-biphenyl]-4-yl)-5,6,11,12-tetraphenyl-2,3-naphthacenediyl]bis- (9CI) (CA INDEX NAME)


Ph
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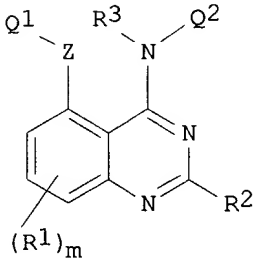
L4 ANSWER 2 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 2001:904160 CAPLUS
DN 136:20087
TI Preparation of 4-anilinoquinazoline derivatives for the treatment of tumors
IN Hennequin, Laurent Francois Andre; Ple, Patrick
PA Astrazeneca Ab, Swed.; Astrazeneca Uk Limited
SO PCT Int. Appl., 234 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001094341	A1	20011213	WO 2001-GB2424	20010601
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRAI	EP 2000-401581	A	20000606		
	EP 2001-400297	A	20010207		
	EP 2001-400565	A	20010305		

OS MARPAT 136:20087
GI



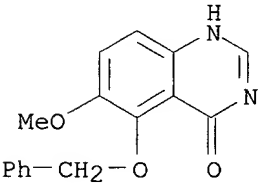
I

AB The invention concerns quinazoline derivs. (I; e.g. 4-(2-chloro-5-methoxyanilino)-7-methoxy-5-(3-morpholinopropoxy)quinazoline (1)), processes for their prepn., pharmaceutical compns. contg. them and their use in the manuf. of a medicament for use as an anti-invasive agent in the containment and/or treatment of solid tumor disease. Although biol. assay methods are described, no test results are reported. It is believed that the antitumor activity is due to inhibition of one or more of the non-receptor tyrosine-specific protein kinases of the Src family that are involved in the signal transduction steps that lead to the invasiveness and migratory ability of metastasizing tumor cells. In I, according to the 1st claim, m = 0-3; each R1 = halo, trifluoromethyl, cyano, isocyano, nitro, hydroxy, mercapto, amino, formyl, carboxy, carbamoyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy,

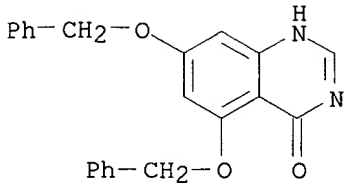
(2-6C)alkynyloxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, (3-6C)alkenoylamino, N-(1-6C)alkyl-(3-6C)alkenoylamino, (3-6C)alkynoylamino, N-(1-6C)alkyl-(3-6C)alkynoylamino, N-(1-6C)alkylsulfamoyl, N,N-di[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino and N-(1-6C)alkyl-(1-6C)alkanesulfonylamino, or Q3-X1- (X1 = direct bond, O, S, SO, SO2, N(R4), CO, CH(OR4), CON(R4), N(R4)CO, SO2N(R4), N(R4)SO2, OC(R4)2, SC(R4)2 and N(R4)C(R4)2 (R4 = H or (1-6C)alkyl) and Q3 = aryl, aryl-(1-6C)alkyl, (3-7C)cycloalkyl, (3-7C)cycloalkyl-, (1-6C)alkyl, (3-7C)cycloalkenyl, (3-7C)cycloalkenyl-(1-6C)alkyl, heteroaryl, heteroaryl-(1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl), or (R1)m is (1-3C)alkylenedioxy, with addnl. optional substitution and/or insertion possible. R2 = H or (1-6C)alkyl; R3 = H or (1-6C)alkyl; Z = direct bond, O, S, SO, SO2, N(R11), CO, CH(OR11), CON(R11), N(R11)CO, SO2N(R11), N(R11)SO2, OC(R11)2, SC(R11)2 and N(R11)C(R11)2 (R11 = H, or (1-6C)alkyl). Q1 = aryl, aryl-(1-6C)alkyl, (3-7C)cycloalkyl, (3-7C)cycloalkyl-(1-6C)alkyl, (3-7C)cycloalkenyl, (3-7C)cycloalkenyl-(1-6C)alkyl, heteroaryl, heteroaryl-(1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl, or, when Z is a direct bond or O, Q1 may be (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, halo-(1-6C)alkyl, hydroxy-(1-6C)alkyl, (1-6C)alkoxy-(1-6C)alkyl, cyano-(1-6C)alkyl, amino-(1-6C)alkyl, (1-6C)alkylamino-(1-6C)alkyl, di[(1-6C)alkyl]amino-(1-6C)alkyl, (1-6C)alkylthio-(1-6C)alkyl, (1-6C)alkylsulfinyl-(1-6C)alkyl or (1-6C)alkylsulfonyl-(1-6C)alkyl, with addnl. optional substitution and/or insertion possible. Q2 = substituted Ph. More than 50 example prepns. are included. For example, 1 was obtained by adding di-tert-Bu azodicarboxylate (0.208 g) dropwise to a stirred mixt. of 4-(2-chloro-5-methoxyanilino)-5-hydroxy-7-methoxyquinazoline (0.2 g), 4-(3-hydroxypropyl)morpholine, PPh3 (0.237 g) and CH2Cl2 (3 mL). The reaction mixt. was stirred at ambient temp. for 1 h.

IT **120075-51-6P**, 5-Benzyloxy-6-methoxy-3,4-dihydroquinazolin-4-one
379228-33-8P, 5,7-Dibenzyloxy-3,4-dihydroquinazolin-4-one
379228-34-9P, 4-(2-Chloro-5-methoxyanilino)-5,7-dibenzyloxyquinazoline hydrochloride
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of anilinoquinazoline derivs. for treatment of tumors)

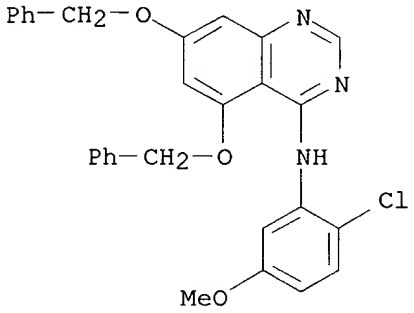
RN 120075-51-6 CAPLUS
CN 4(1H)-Quinazolinone, 6-methoxy-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



RN 379228-33-8 CAPLUS
CN 4(1H)-Quinazolinone, 5,7-bis(phenylmethoxy)- (9CI) (CA INDEX NAME)

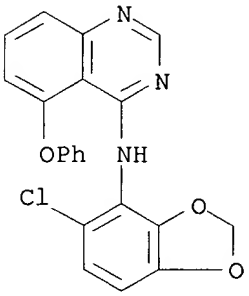


RN 379228-34-9 CAPLUS
CN 4-Quinazolinamine, N-(2-chloro-5-methoxyphenyl)-5,7-bis(phenylmethoxy)-, hydrochloride (9CI) (CA INDEX NAME)



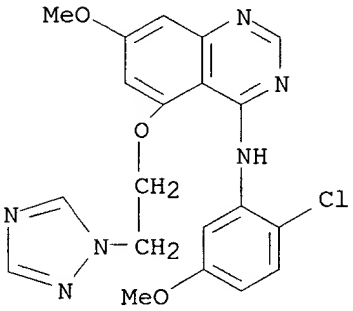
● x HCl

IT **379230-67-8P**, 4-(6-Chloro-2,3-methylenedioxyanilino)-5-phenoxyquinazoline monohydrochloride **379231-11-5P**, 4-(2-Chloro-5-methoxyanilino)-7-methoxy-5-(2-(1,2,4-triazol-1-yl)ethoxy)quinazoline **379231-16-0P**, 4-(2-Chloro-5-methoxyanilino)-5-(2-(imidazol-1-yl)ethoxy)quinazoline dihydrochloride
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of anilinoquinazoline derivs. for treatment of tumors)
RN 379230-67-8 CAPLUS
CN 4-Quinazolinamine, N-(5-chloro-1,3-benzodioxol-4-yl)-5-phenoxy-, monohydrochloride (9CI) (CA INDEX NAME)

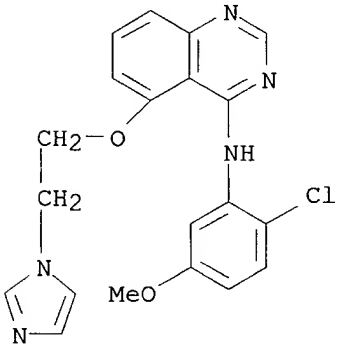


● HCl

RN 379231-11-5 CAPLUS
CN 4-Quinazolinamine, N-(2-chloro-5-methoxyphenyl)-7-methoxy-5-[2-(1H-1,2,4-triazol-1-yl)ethoxy]- (9CI) (CA INDEX NAME)



RN 379231-16-0 CAPLUS
CN 4-Quinazolinamine, N-(2-chloro-5-methoxyphenyl)-5-[2-(1H-imidazol-1-yl)ethoxy]-, dihydrochloride (9CI) (CA INDEX NAME)



2 HCl

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 2001:661418 CAPLUS
DN 135:216011
TI preparation of 4-amino-6,7-dimethoxy-2-(5-methanesulfonamido-1,2,3,4-tetrahydroisoquinol-2-yl)-5-(2-pyridyl)quinazoline mesylate and polymorphs
IN Basford, Patricia Ann; Hodgson, Paul Blaise
PA Pfizer Limited, UK; Pfizer Inc.
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001064672	A1	20010907	WO 2001-IB244	20010223
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002010188	A1	20020124	US 2001-797112	20010301
PRAI	GB 2000-5200	A	20000303		
	GB 2000-15900	A	20000628		
	US 2000-192912P	P	20000329		
	US 2000-218188P	P	20000714		

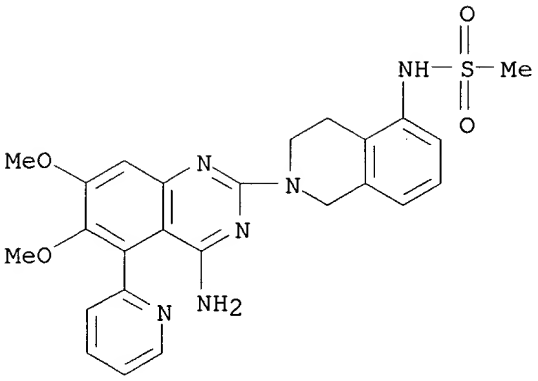
AB The polymorphs of 4-amino-6,7-dimethoxy-2-(5-methanesulfonamido-1,2,3,4-tetrahydroisoquinol-2-yl)-5-(2-pyridyl)quinazoline mesylate (I) are disclosed. The invention also relates to substantially pure anhyd. cryst. polymorphic forms of the free base. The compds. are particularly useful in the treatment of benign prostatic hyperplasia. Thus, polymorphs I were prepd. by the reaction of 4-amino-6,7-dimethoxy-2-chloro-5-(2-pyridyl)quinazoline with N-(1,2,3,4-tetrahydro-5-isoquinolyl)methanesulfonamide-HCl in the presence of Et3N.

IT **358632-25-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aminomethanesulfonamido(tetrahydroisoquinolyl)(pyridyl)quinazoline mesylate and polymorphs)

RN 358632-25-4 CAPLUS
CN Methanesulfonamide, N-[2-[4-amino-6,7-dimethoxy-5-(2-pyridinyl)-2-quinazolinyl]-1,2,3,4-tetrahydro-5-isoquinolinyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

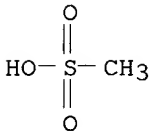
CM 1

CRN 210538-44-6
CMF C25 H26 N6 O4 S

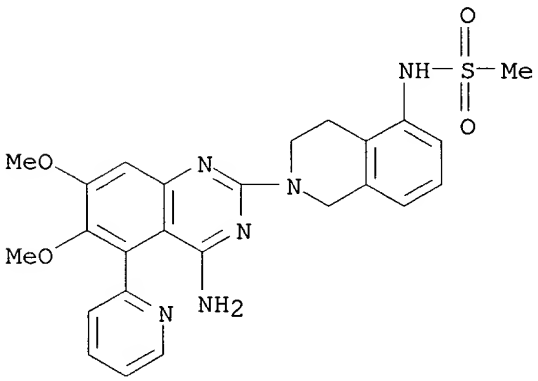


CM 2

CRN 75-75-2
CMF C H4 O3 S

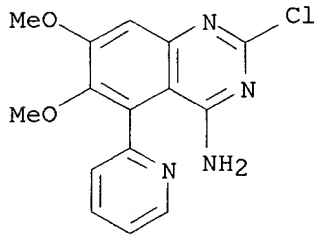


IT **210538-44-6P**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aminomethanesulfonamido(tetrahydroisoquinolyl)(pyridyl)quinazoline mesylate and polymorphs)
RN 210538-44-6 CAPLUS
CN Methanesulfonamide, N-[2-[4-amino-6,7-dimethoxy-5-(2-pyridinyl)-2-quinazolinyl]-1,2,3,4-tetrahydro-5-isoquinolinyl]- (9CI) (CA INDEX NAME)



IT **210538-70-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of aminomethanesulfonamido(tetrahydroisoquinolyl)(pyridyl)quina

zoline mesylate and polymorphs)
RN 210538-70-8 CAPLUS
CN 4-Quinazolinamine, 2-chloro-6,7-dimethoxy-5-(2-pyridinyl)- (9CI) (CA INDEX NAME)



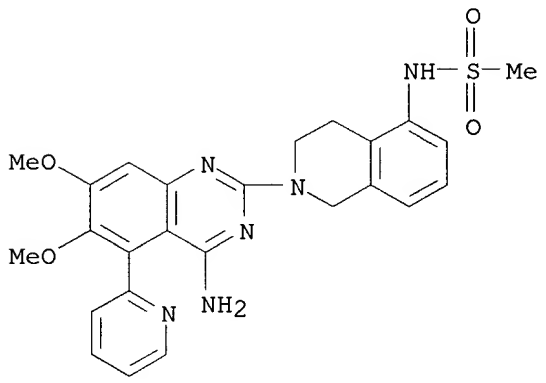
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 2001:594376 CAPLUS
DN 135:185453
TI Pharmaceutical combinations for treating lower urinary tract disfunctions
IN Wyllie, Michael Grant
PA Pfizer Products Inc., USA
SO Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1123705	A1	20010816	EP 2001-301085	20010207
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 2001044438	A1	20011122	US 2001-778290	20010207
PRAI	US 2000-181310P	P	20000209		

AB Pharmaceutical combinations suitable for treating the lower urinary tract symptoms assocd. with benign prostatic hyperplasia in men contain an .alpha.-adrenoceptor antagonist and a muscarinic antagonist. The combinations of the invention are particularly suitable for treating moderate or severe lower urinary tract symptoms. Thus, tablet contained doxazosin mesylate 4.05, microcryst. cellulose 125.28, lactose 66.67, sodium starch glycolate 2.00, and Mg stearate 2.00% by wt.

IT **210538-44-6**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical combinations for treating lower urinary tract disfunctions)
RN 210538-44-6 CAPLUS
CN Methanesulfonamide, N-[2-[4-amino-6,7-dimethoxy-5-(2-pyridinyl)-2-quinazolinyl]-1,2,3,4-tetrahydro-5-isoquinolinyl]- (9CI) (CA INDEX NAME)

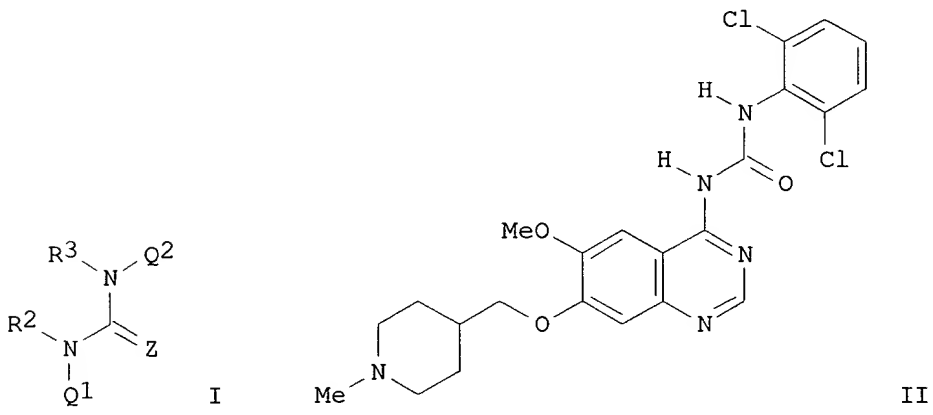


RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 2001:50631 CAPLUS
DN 134:100885
TI Preparation of quinazolinyl ureas, thioureas and guanidines for use in the prevention or treatment of T cell mediated diseases or medical conditions
IN Crawley, Graham Charles; McKerrecher, Darren; Poyser, Jeffrey Philip; Hennequin, Laurent Francois Andre; Ple, Patrick; Lambert, Christine Marie-Paul
PA Astrazeneca UK Limited, UK; Zeneca Pharma S.A.
SO PCT Int. Appl., 169 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001004102	A1	20010118	WO 2000-GB2566	20000704
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	BR 2000012157	A	20020402	BR 2000-12157	20000704
	EP 1218353	A1	20020703	EP 2000-953271	20000704
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	NO 2002000042	A	20020304	NO 2002-42	20020104
PRAI	EP 1999-401692	A	19990707		
	EP 2000-401221	A	20000504		
	WO 2000-GB2566	W	20000704		

OS MARPAT 134:100885
GI



AB The title compds. [I; Q1 = quinazoline ring optionally substituted with

halo, CF3 or CN, or a group X1Q3 (wherein X1 = a direct bond, O; Q3 = aryl, arylalkyl, heterocyclyl, (heterocyclyl)alkyl); R2, R3 = H, alkyl; Z = O, S, NH; Q2 = aryl, arylalkyl] and their pharmaceutically-acceptable salts, useful in the prevention or treatment of T cell mediated diseases or medical conditions such as transplant rejection or rheumatoid arthritis, were prepd. and formulated. E.g., a multi-step synthesis of the urea II was given. In general, activity possessed by compds. I may be demonstrated at IC50 of 0.0001- 5 .mu.M against enzyme p56lck binding and IC50 of 0.001-10 .mu.M in in vitro T cell proliferation assay (T cell receptor stimulation).

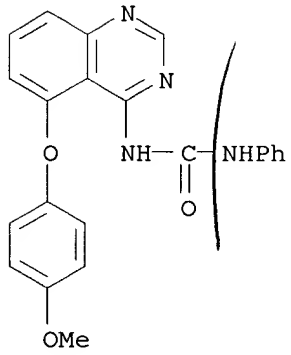
IT **212632-65-0 212632-66-1 212632-67-2**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(prepn. of quinazolinyl ureas, thioureas and guanidines for use in the prevention or treatment of T cell mediated diseases or medical conditions)

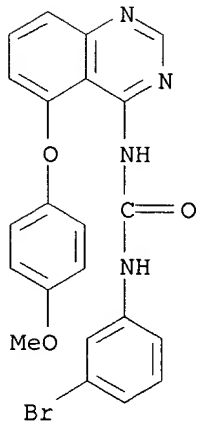
RN 212632-65-0 CAPLUS

CN Urea, N-[5-(4-methoxyphenoxy)-4-quinazolinyl]-N'-phenyl- (9CI) (CA INDEX NAME)

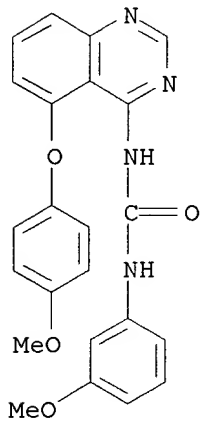


RN 212632-66-1 CAPLUS

CN Urea, N-(3-bromophenyl)-N'-[5-(4-methoxyphenoxy)-4-quinazolinyl]- (9CI) (CA INDEX NAME)



RN 212632-67-2 CAPLUS
CN Urea, N-[5-(4-methoxyphenoxy)-4-quinazolinyl]-N'-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)

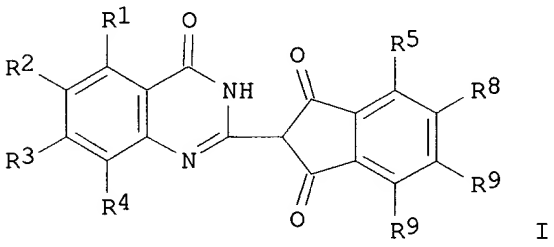


RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 6 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 2000:712847 CAPLUS
DN 133:288936
TI Rewritable laser recording medium including tautomeric .gamma.-quinazolone derivative
IN Ogiso, Akira; Tsukahara, Hiroshi; Nishimoto, Taizo; Misawa, Tsutayoshi; Takuma, Keisuke
PA Mitsui Chemical Industry Co., Ltd., Japan; Yamamoto Chemicals Inc.
SO Jpn. Kokai Tokkyo Koho, 22 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000280620	A2	20001010	JP 1999-89012	19990330

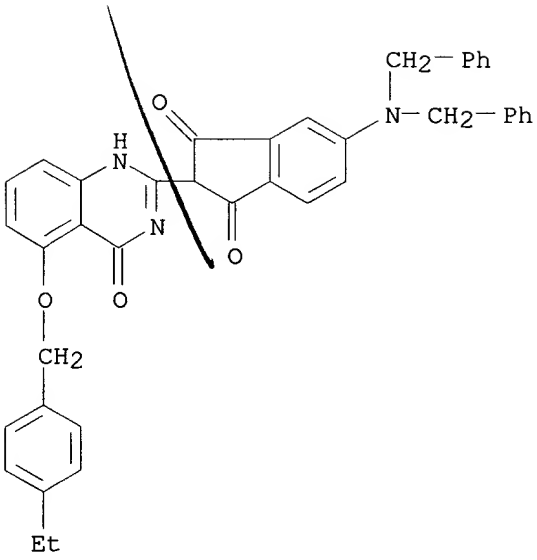
OS MARPAT 133:288936
GI



I

AB The medium, suited for ultrahigh-d. recording by blue laser light (400-500 nm wavelength), includes a recording layer contg. a tautomeric .gamma.-quinazolone deriv. I (R1-8 = H, halo, substituents).

IT **300364-29-8**
RL: DEV (Device component use); USES (Uses)
(rewritable optical recording medium including tautomeric .gamma.-quinazolone deriv. for high-d. laser recording)
RN 300364-29-8 CAPLUS
CN 1H-Indene-1,3(2H)-dione, 5-[bis(phenylmethyl)amino]-2-[5-[(4-ethylphenyl)methoxy]-1,4-dihydro-4-oxo-2-quinazolinyl]- (9CI) (CA INDEX NAME)

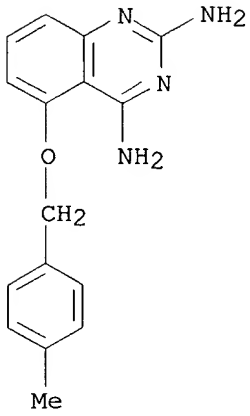

CH2— Ph
N— CH2— Ph
O
H
N
N
O
O
O
CH2
Et

L1 ANSWER 7 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 2000:529192 CAPLUS
DN 133:131727
TI Mammalian DNA primase screens and activity modulating agents
IN Kozlowski, Michael; Aimi, Junko
PA Geron Corporation, USA
SO U.S., 21 pp., Cont.-in-part of U.S. Ser. No. 624,343, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6096499	A	20000801	US 1997-828192	19970321
	US 6274738	B1	20010814	US 1997-977651	19971124
PRAI	US 1996-624343	B2	19960322		
	US 1997-828192	A2	19970321		

AB The invention provides DNA primase assays suitable for identifying DNA primase modulating agents, methods of modulating DNA primase activity and compns. which modulate DNA primase. In one assay of the invention, a probe is hybridized to a primase reaction product, with the amt. of probe bound providing a measure of activity for the primase enzyme. The probe or product may be immobilized or captured on a solid surface, which is optionally washed to remove non-specifically bound components after hybridization with primase reaction products or probes in the products. Optionally, the assay includes a blocking agent, such as albumin, a nonfat milk protein, polyvinyl pyrrolidone, or Ficoll. The assay identifies DNA primase modifiers which produce: (1) a detectable alteration in DNA primase activity, such as the capacity of a DNA primase to initiate oligoribonucleotide primer synthesis and/or the rate of chain elongation of a nascent oligoribonucleotide primer catalyzed by DNA primase either alone or in conjunction with DNA polymerase .alpha.; and/or (2) a detectable alteration in the capacity or rate of a DNA primase/DNA polymerase complex to extend oligoribonucleotide primers by template-directed addn. of deoxyribonucleotides; and/or (3) a detectable alteration in the binding capacity, binding affinity, or functional interaction between a DNA primase and an accessory protein.

IT **215925-77-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(primase modulator; mammalian DNA primase screens and activity modulating agents)
RN 215925-77-2 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(4-methylphenyl)methoxy]- (9CI) (CA INDEX NAME)



RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 8 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 2000:277883 CAPLUS
DN 132:318052
TI Modulation of gene expression by combination therapy with antisense oligonucleotide and gene product protein effector
IN Besterman, Jeffrey M.; Macleod, Alan Robert; Siders, William M.
PA Methylgene, Inc., Can.
SO PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

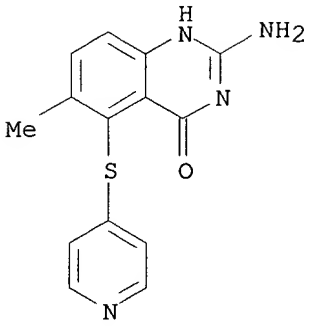
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000023112	A1	20000427	WO 1999-US24278	19991019
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9965194	A1	20000508	AU 1999-65194	19991019
EP 1123111	A1	20010816	EP 1999-953211	19991019
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRAI US 1998-104804P P 19981019
WO 1999-US24278 W 19991019

AB The invention relates to the modulation of gene expression. In particular, the invention relates to compns. comprising antisense oligonucleotides which inhibit expression of a gene in operable assocn. with protein effectors of a product of that gene, and methods of using the same. In addn., the invention relates to the modulation of mammalian gene expression regulated by methylation.

IT **152946-68-4**, Thymitaq
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antisense oligonucleotide and gene product protein effector for gene expression modulation)

RN 152946-68-4 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)



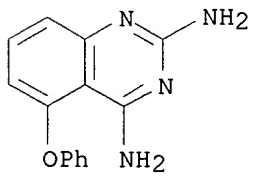
●2 HCl

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 9 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 2000:84619 CAPLUS
DN 132:117566
TI Small molecule inhibitors of Bcl-2 proteins for inducing apoptosis
IN Huang, Ziwei; Lui, Dongxiang; Han, Xiaobing; Zhang, Zhijia; Wang, Jialun
PA Thomas Jefferson University, USA
SO PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000004901	A1	20000203	WO 1999-US12384	19990720
	W: CA, JP				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 1100496	A1	20010523	EP 1999-937146	19990720
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI US 1998-93561P P 19980721
US 1999-128100P P 19990407
WO 1999-US12384 W 19990720
OS MARPAT 132:117566
AB Small mol. inhibitors of Bcl-2 function are used to induce apoptosis of cells which are subject to Bcl-2, which cells are otherwise subject to Bcl-2-mediated blockage of apoptosis. The compds. are useful for treating cancer, autoimmune disorders and viral infection. The binding to Bcl-2 protein of 716 org. compds. selected from computer screening studies were initially tested at 100 .mu.M concn. A group of compds. was found to be active in the Bcl-2 ligand binding assay with a level of inhibition ranging from 35% to 98%. Four of the active compds., designated as HA01 (HA12-16), HA02, HA03, and HA04, showed a concn.-dependent competition binding. The two most potent compds., HA01 and HA02, exhibited a binding affinity (KD) of 7 .mu.M and 15 .mu.M, resp. Compd. HA14-1 was tested in the same manner. A clear concn.-dependent competition binding was obsd. for this compd. over a concn. of 1-100 .mu.M. Also, the compds. HA01, HA02 and HA04 induced apoptosis in a human pre-B leukemia cell line (697 cells) using taxol as a pos. control.
IT **123241-96-3**, HA 04
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(apoptosis induced by inhibitors of Bcl-2 protein for treatment of autoimmune disorders, cancer, and viral infection)
RN 123241-96-3 CAPLUS
CN 2,4-Quinazolinediamine, 5-phenoxy- (9CI) (CA INDEX NAME)



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

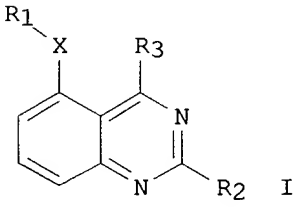
ALL CITATIONS AVAILABLE IN THE RE FORMAT

applicants

L14 ANSWER 10 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1998:745041 CAPLUS
DN 130:10618
TI Modulating serine/threonine protein kinase function with quinazoline-based compounds and their use as antitumor and anti-fibrotic agents
IN Tang, Peng C.; McMahon, Gerald; Weinberger, Heinz; Kutscher, Bernhard; App, Harald
PA Sugen, Inc., USA
SO PCT Int. Appl., 147 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9850370	A1	19981112	WO 1998-US9060	19980501
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	ZA 9803669	A	19991101	ZA 1998-3669	19980430
	AU 9872829	A1	19981127	AU 1998-72829	19980501
	EP 981519	A1	20000301	EP 1998-920203	19980501
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 6204267	B1	20010320	US 1998-71682	19980501
	JP 2001524128	T2	20011127	JP 1998-548336	19980501
	US 2001014679	A1	20010816	US 2001-769360	20010126
PRAI	US 1997-45351P	P	19970502		
	US 1997-60152P	P	19970926		
	US 1998-71682	A3	19980501		
	WO 1998-US9060	W	19980501		

OS CASREACT 130:10618; MARPAT 130:10618
GI



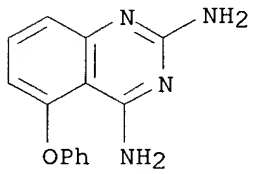
I

AB The present invention is directed in part towards methods of modulating the function of serine/threonine protein kinases with quinazoline-based compds (I). The methods incorporate cells that express a serine/threonine protein kinase, such as RAF. In addn., the invention describes methods of preventing and treating serine/threonine protein kinase-related abnormal conditions (e.g., tumors, fibrotic disorders, or other signal transduction aberrations) in organisms with a compd. identified by the invention. Furthermore, the invention pertains to quinazoline compds. and

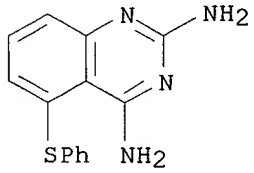
pharmaceutical compns. comprising these compds. Syntheses and biol. activities are are provided for 38 quinazoline-based compds.

IT **123241-96-3P 123241-99-6P 168910-32-5P**
168910-48-3P 212632-64-9P 212632-66-1P
212632-67-2P 212632-68-3P 212632-69-4P
212632-71-8P 212632-72-9P 212632-74-1P
215925-67-0P 215925-68-1P 215925-69-2P
215925-70-5P 215925-71-6P 215925-72-7P
215925-73-8P 215925-74-9P 215925-75-0P
215925-76-1P 215925-77-2P 215925-78-3P
215925-80-7P 215925-81-8P 215925-82-9P
215925-83-0P 215925-84-1P 215925-85-2P
215925-86-3P 215925-87-4P 215925-88-5P
215925-89-6P 215925-90-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(modulating serine/threonine protein kinase function with quinazoline-based compds. and their use as antitumor and anti-fibrotic agents)

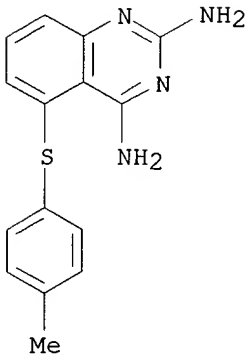
RN 123241-96-3 CAPLUS
CN 2,4-Quinazolinediamine, 5-phenoxy- (9CI) (CA INDEX NAME)



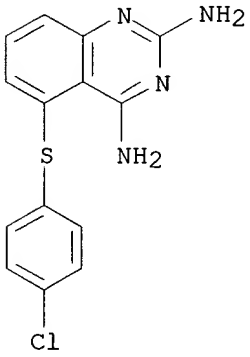
RN 123241-99-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-(phenylthio)- (9CI) (CA INDEX NAME)



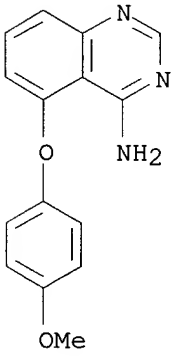
RN 168910-32-5 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(4-methylphenyl)thio]- (9CI) (CA INDEX NAME)



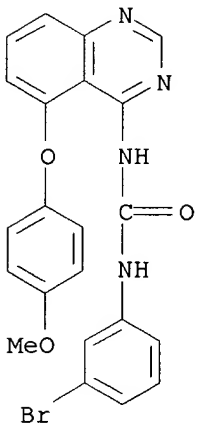
RN 168910-48-3 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(4-chlorophenyl)thio]- (9CI) (CA INDEX NAME)



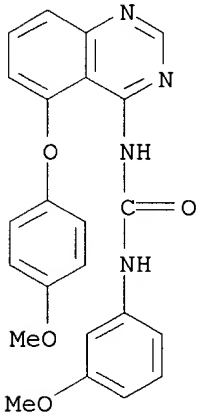
RN 212632-64-9 CAPLUS
CN 4-Quinazolinamine, 5-(4-methoxyphenoxy)- (9CI) (CA INDEX NAME)



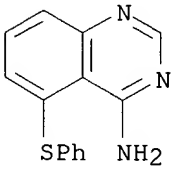
RN 212632-66-1 CAPLUS
CN Urea, N-(3-bromophenyl)-N'-[5-(4-methoxyphenoxy)-4-quinazolinyl]- (9CI) (CA INDEX NAME)



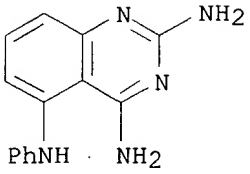
RN 212632-67-2 CAPLUS
CN Urea, N-[5-(4-methoxyphenoxy)-4-quinazolinyl]-N'-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



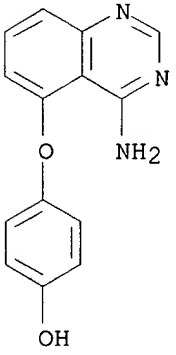
RN 212632-68-3 CAPLUS
CN 4-Quinazolinamine, 5-(phenylthio)- (9CI) (CA INDEX NAME)



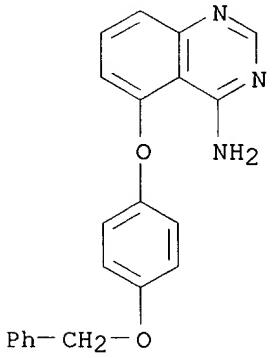
RN 212632-69-4 CAPLUS
CN 2,4,5-Quinazolinetriamine, N5-phenyl- (9CI) (CA INDEX NAME)



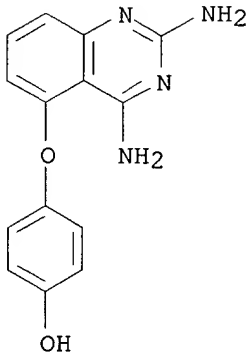
RN 212632-71-8 CAPLUS
CN Phenol, 4-[(4-amino-5-quinazolinyl)oxy]- (9CI) (CA INDEX NAME)



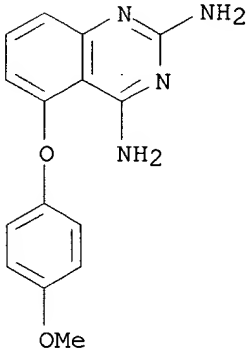
RN 212632-72-9 CAPLUS
CN 4-Quinazolinamine, 5-[4-(phenylmethoxy)phenoxy]- (9CI) (CA INDEX NAME)



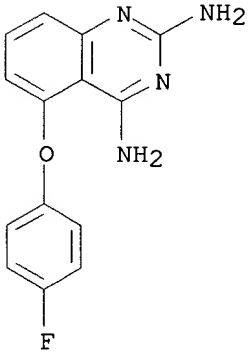
RN 212632-74-1 CAPLUS
CN Phenol, 4-[(2,4-diamino-5-quinazolinyl)oxy]- (9CI) (CA INDEX NAME)



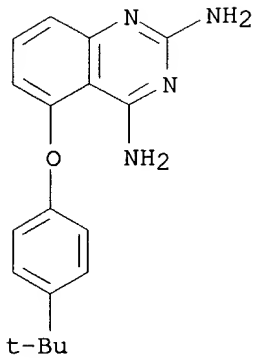
RN 215925-67-0 CAPLUS
CN 2,4-Quinazolinediamine, 5-(4-methoxyphenoxy)- (9CI) (CA INDEX NAME)



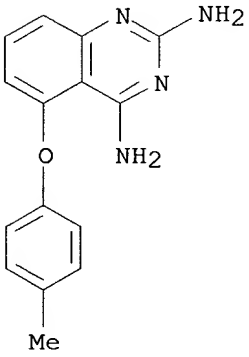
RN 215925-68-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-(4-fluorophenoxy)- (9CI) (CA INDEX NAME)



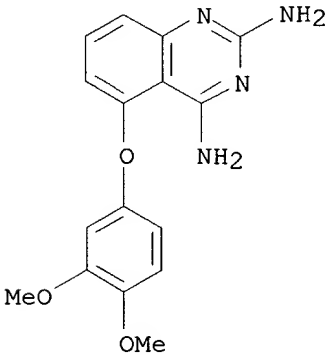
RN 215925-69-2 CAPLUS
CN 2,4-Quinazolinediamine, 5-[4-(1,1-dimethylethyl)phenoxy]- (9CI) (CA INDEX NAME)



RN 215925-70-5 CAPLUS
CN 2,4-Quinazolinediamine, 5-(4-methylphenoxy)- (9CI) (CA INDEX NAME)



RN 215925-71-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-(3,4-dimethoxyphenoxy)- (9CI) (CA INDEX NAME)



RN 215925-72-7 CAPLUS
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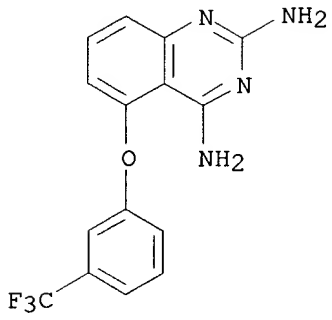
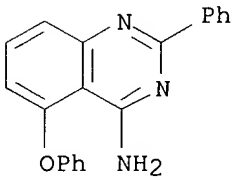
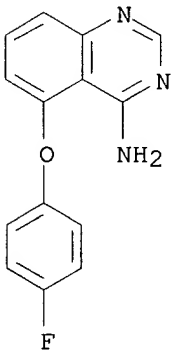


RN 215925-73-8 CAPLUS
CN 4-Quinazolinamine, 5-phenoxy-2-phenyl- (9CI) (CA INDEX NAME)



RN 215925-74-9 CAPLUS
CN 4-Quinazolinamine, 5-(4-fluorophenoxy)- (9CI) (CA INDEX NAME)



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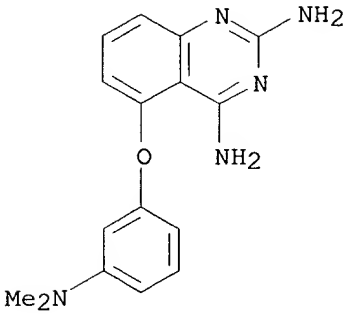
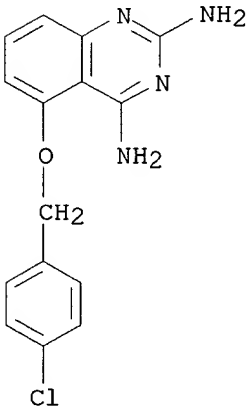
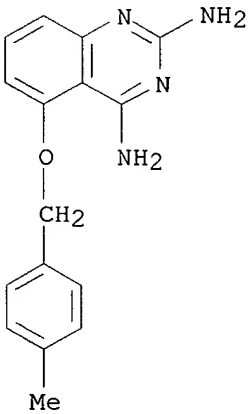
CN 2,4-Quinazolinediamine, 5-[3-(dimethylamino)phenoxy]- (9CI) (CA INDEX NAME)



RN 215925-76-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(4-chlorophenyl)methoxy]- (9CI) (CA INDEX NAME)



RN 215925-77-2 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(4-methylphenyl)methoxy]- (9CI) (CA INDEX NAME)



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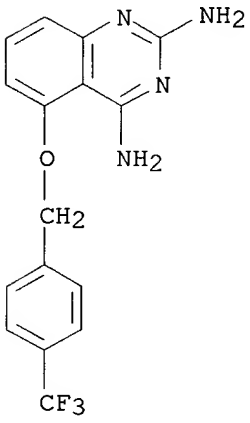
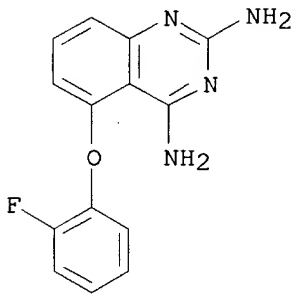
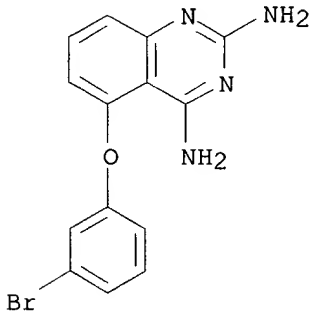
CN 2,4-Quinazolinediamine, 5-[[4-(trifluoromethyl)phenyl]methoxy]- (9CI) (CA INDEX NAME)



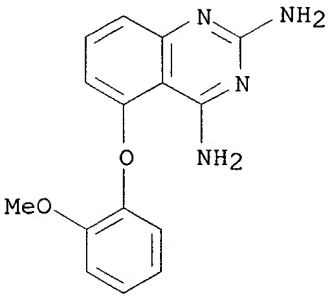
RN 215925-80-7 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-fluorophenoxy)- (9CI) (CA INDEX NAME)



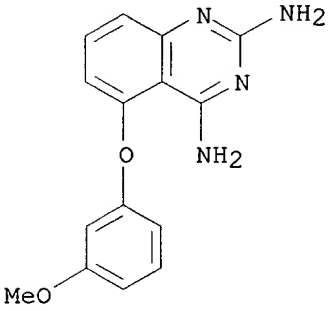
RN 215925-81-8 CAPLUS
CN 2,4-Quinazolinediamine, 5-(3-bromophenoxy)- (9CI) (CA INDEX NAME)



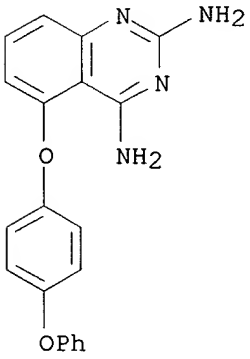
RN 215925-82-9 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-methoxyphenoxy)- (9CI) (CA INDEX NAME)



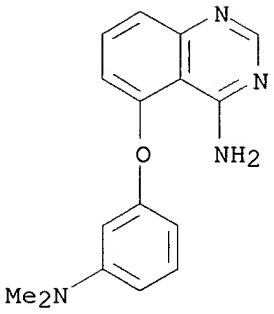
RN 215925-83-0 CAPLUS
CN 2,4-Quinazolinediamine, 5-(3-methoxyphenoxy)- (9CI) (CA INDEX NAME)



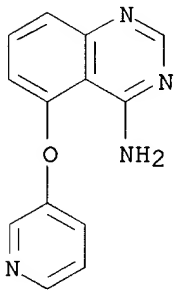
RN 215925-84-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-(4-phenoxyphenoxy)- (9CI) (CA INDEX NAME)



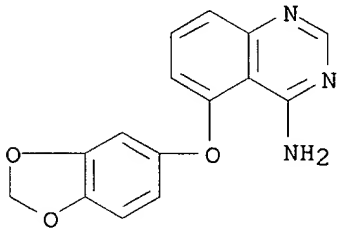
RN 215925-85-2 CAPLUS
CN 4-Quinazolinamine, 5-[3-(dimethylamino)phenoxy]- (9CI) (CA INDEX NAME)



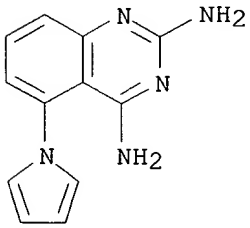
RN 215925-86-3 CAPLUS
CN 4-Quinazolinamine, 5-(3-pyridinyloxy)- (9CI) (CA INDEX NAME)



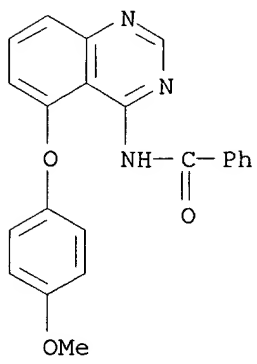
RN 215925-87-4 CAPLUS
CN 4-Quinazolinamine, 5-(1,3-benzodioxol-5-yloxy)- (9CI) (CA INDEX NAME)



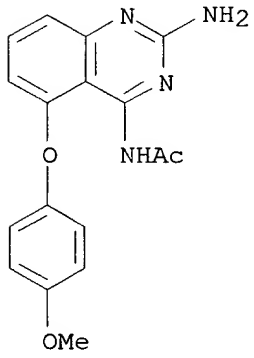
RN 215925-88-5 CAPLUS
CN 2,4-Quinazolinediamine, 5-(1H-pyrrol-1-yl)- (9CI) (CA INDEX NAME)



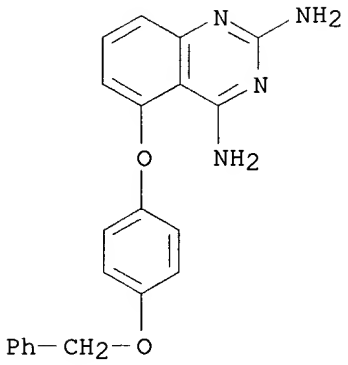
RN 215925-89-6 CAPLUS
CN Benzamide, N-[5-(4-methoxyphenoxy)-4-quinazolinyl]- (9CI) (CA INDEX NAME)



RN 215925-90-9 CAPLUS
CN Acetamide, N-[2-amino-5-(4-methoxyphenoxy)-4-quinazolinyl]- (9CI) (CA INDEX NAME)



IT **212632-73-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(modulating serine/threonine protein kinase function with quinazoline-based compds. and their use as antitumor and anti-fibrotic agents)
RN 212632-73-0 CAPLUS
CN 2,4-Quinazolinediamine, 5-[4-(phenylmethoxy)phenoxy]- (9CI) (CA INDEX NAME)

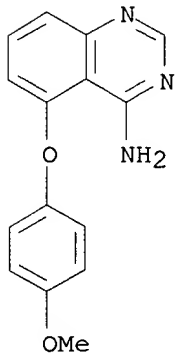


RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

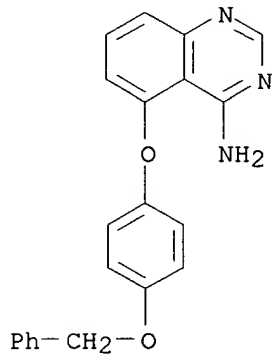
L4 ANSWER 11 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1998:612013 CAPLUS
DN 129:221202
TI Formulations for hydrophobic pharmaceutical agents
IN Shenoy, Narmada; Wagner, Gregory S.
PA Sugen, Inc., USA
SO PCT Int. Appl., 135 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9838984	A2	19980911	WO 1998-US4134	19980304
	WO 9838984	A3	19990128		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9866806	A1	19980922	AU 1998-66806	19980304
	AU 743024	B2	20020117		
	EP 1014953	A2	20000705	EP 1998-908884	19980304
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 6248771	B1	20010619	US 1998-34374	19980304
	JP 2001514626	T2	20010911	JP 1998-538698	19980304
	US 2001012844	A1	20010809	US 2001-797842	20010305
PRAI	US 1997-39870P	P	19970305		
	US 1997-41251P	P	19970318		
	US 1998-34374	A3	19980304		
	WO 1998-US4134	W	19980304		

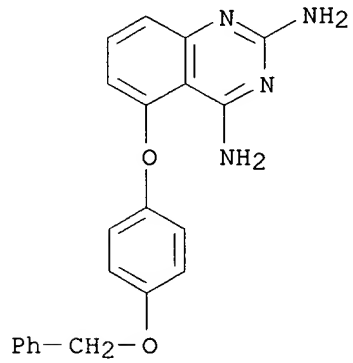
OS MARPAT 129:221202
AB The present invention features formulations, including liq., semi-solid or solid pharmaceutical formulations, that improve the oral bioavailability of hydrophobic pharmaceutical agents, such as quinazoline-, nitrothiazole-, and indolinone-based compds. Also featured are formulations for parenteral delivery of such hydrophobic pharmaceutical agents, as well as methods of making and using both types of formulations. A claimed formulation comprises the hydrophobic pharmaceutical agents, polyoxyhydrocarbyl compds, and surfactants. A parenteral soln. contained 3-[(2,4-dimethylpyrrol-5-yl)methylene]-2-indolinone 5, PEG-400 35, Cremophor EL 25, benzyl alc. 2, ethanol 11.4, and sterile water to 100 % wt./vol.
IT **212632-64-9 212632-72-9 212632-73-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of hydrophobic quinazoline drugs in; formulations for hydrophobic drugs contg. polyoxyhydrocarbyl compds. and surfactants to improve soly.)
RN 212632-64-9 CAPLUS
CN 4-Quinazolinamine, 5-(4-methoxyphenoxy)- (9CI) (CA INDEX NAME)



RN 212632-72-9 CAPLUS
CN 4-Quinazolinamine, 5-[4-(phenylmethoxy)phenoxy]- (9CI) (CA INDEX NAME)



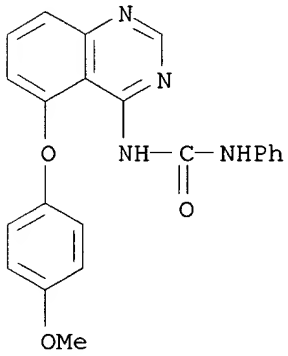
RN 212632-73-0 CAPLUS
CN 2,4-Quinazolinediamine, 5-[4-(phenylmethoxy)phenoxy]- (9CI) (CA INDEX NAME)



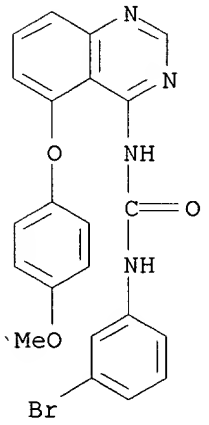
IT **212632-65-0P 212632-66-1P 212632-67-2P**
212632-68-3P 212632-69-4P 212632-70-7P
212632-71-8P 212632-74-1P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological

study); PREP (Preparation); USES (Uses)
(prepn. of hydrophobic quinazoline drugs in; formulations for hydrophobic drugs contg. polyoxyhydrocarbyl compds. and surfactants to improve soly.)

RN 212632-65-0 CAPLUS
CN Urea, N-[5-(4-methoxyphenoxy)-4-quinazolinyl]-N'-phenyl- (9CI) (CA INDEX NAME)



RN 212632-66-1 CAPLUS
CN Urea, N-(3-bromophenyl)-N'-[5-(4-methoxyphenoxy)-4-quinazolinyl]- (9CI) (CA INDEX NAME)



RN 212632-67-2 CAPLUS
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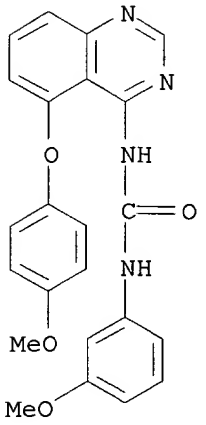
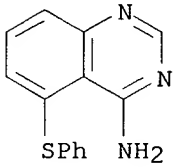
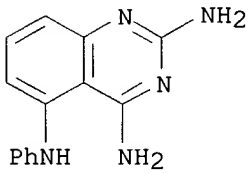


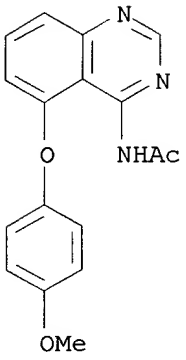
RN 212632-68-3 CAPLUS
CN 4-Quinazolinamine, 5-(phenylthio)- (9CI) (CA INDEX NAME)



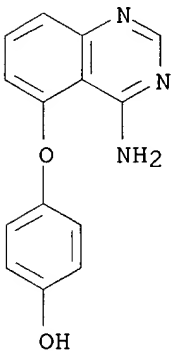
RN 212632-69-4 CAPLUS
CN 2,4,5-Quinazolinetriamine, N5-phenyl- (9CI) (CA INDEX NAME)



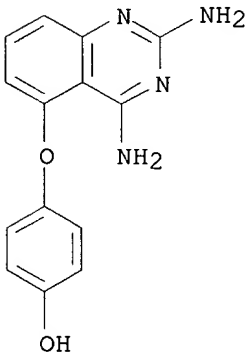
RN 212632-70-7 CAPLUS
CN Acetamide, N-[5-(4-methoxyphenoxy)-4-quinazolinyl]- (9CI) (CA INDEX NAME)



RN 212632-71-8 CAPLUS
CN Phenol, 4-[(4-amino-5-quinazolinyl)oxy]- (9CI) (CA INDEX NAME)



RN 212632-74-1 CAPLUS
CN Phenol, 4-[(2,4-diamino-5-quinazolinyl)oxy]- (9CI) (CA INDEX NAME)



L14 ANSWER 12 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1998:490639 CAPLUS
DN 129:136176
TI Quinoline and quinazoline compounds useful in therapy, particularly in the treatment of benign prostatic hyperplasia
IN Fox, David Nathan Abraham
PA Pfizer Ltd., UK; Pfizer Inc.; Fox, David Nathan Abraham
SO PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9830560	A1	19980716	WO 1998-EP143	19980106
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9862088	A1	19980803	AU 1998-62088	19980106
	AU 724990	B2	20001005		
	EP 968208	A1	20000105	EP 1998-904058	19980106
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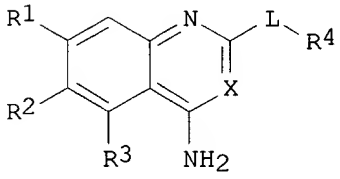
	BR 9807068	A	20000502	BR 1998-7068	19980106
	JP 2000507966	T2	20000627	JP 1998-530565	19980106
	ZA 9800166	A	19990709	ZA 1998-166	19980109
	US 6169093	B1	20010102	US 1999-341228	19990707
	NO 9903396	A	19990709	NO 1999-3396	19990709
	US 6365599	B1	20020402	US 2000-586503	20000602
	US 2002040028	A1	20020404	US 2001-7753	20011113
PRAI	GB 1997-504	A	19970111		
	WO 1998-EP143	W	19980106		
	US 1999-341228	A3	19990707		
	US 2000-586503	A3	20000602		

OS MARPAT 129:136176
GI



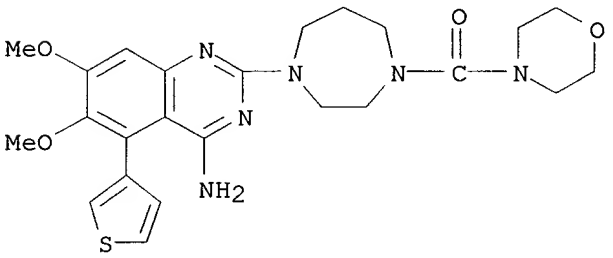
I

AB I [R1 = C1-4 alkoxy optionally substituted by one or more fluorine atoms; R2 = H, C1-6 alkoxy optionally substituted by one or more fluorine atoms; R3 = 5- or 6-membered heterocyclic ring, the ring being optionally substituted; R4 = 4-, 5-, 6- or 7-membered heterocyclic ring, the ring

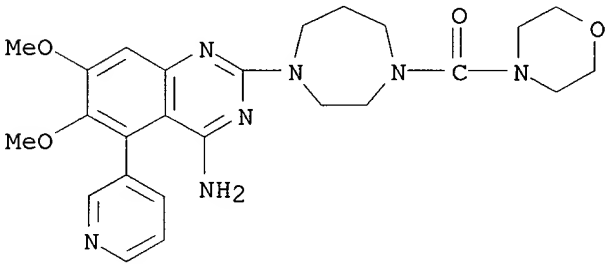
being optionally fused to a benzene ring or a 5- or 6-membered heterocyclic ring, the ring system as a whole being optionally substituted; X = CH, N; L is absent or represents a N-contg. cyclic group or chain], useful in treatment of benign prostatic hyperplasia, were prepd. E.g., 4-amino-6,7-dimethoxy-2-[4-(4-morpholinecarbonyl)-1,4-diazepan-1-yl]-5-(oxazol-2-yl)quinoline was prepd.

IT **210538-18-4P 210538-20-8P 210538-22-0P**
210538-24-2P 210538-26-4P 210538-28-6P
210538-30-0P 210538-32-2P 210538-34-4P
210538-36-6P 210538-38-8P 210538-40-2P
210538-42-4P 210538-44-6P 210538-46-8P
210538-47-9P 210538-48-0P 210538-59-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of quinoline and quinazoline derivs. useful in treatment of benign prostatic hyperplasia)

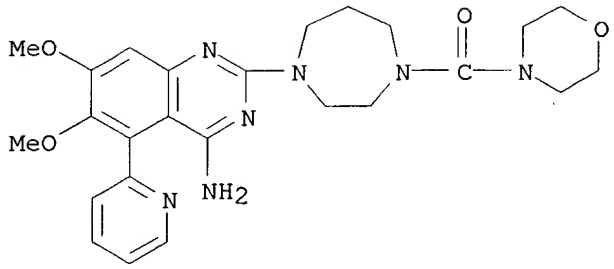
RN 210538-18-4 CAPLUS
CN 1H-1,4-Diazepine, 1-[4-amino-6,7-dimethoxy-5-(3-thienyl)-2-quinazolinyl]hexahydro-4-(4-morpholinylcarbonyl)- (9CI) (CA INDEX NAME)



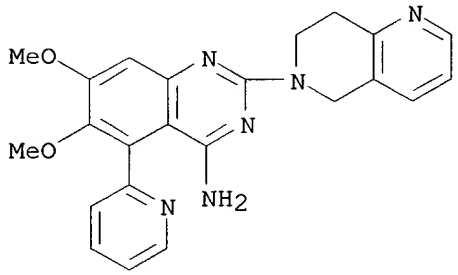
RN 210538-20-8 CAPLUS
CN 1H-1,4-Diazepine, 1-[4-amino-6,7-dimethoxy-5-(3-pyridinyl)-2-quinazolinyl]hexahydro-4-(4-morpholinylcarbonyl)- (9CI) (CA INDEX NAME)



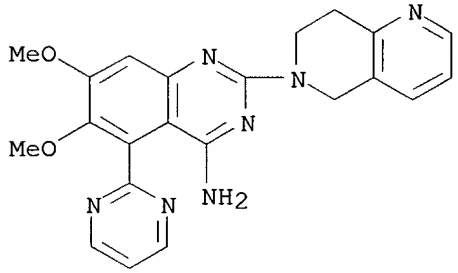
RN 210538-22-0 CAPLUS
CN 1H-1,4-Diazepine, 1-[4-amino-6,7-dimethoxy-5-(2-pyridinyl)-2-quinazolinyl]hexahydro-4-(4-morpholinylcarbonyl)- (9CI) (CA INDEX NAME)



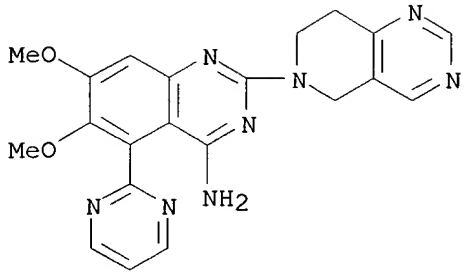
RN 210538-24-2 CAPLUS
CN 4-Quinazolinamine, 2-(7,8-dihydro-1,6-naphthyridin-6(5H)-yl)-6,7-dimethoxy-5-(2-pyridinyl)- (9CI) (CA INDEX NAME)



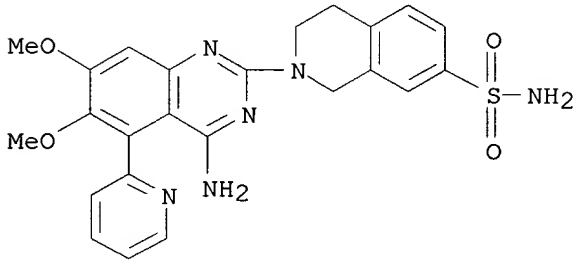
RN 210538-26-4 CAPLUS
CN 4-Quinazolinamine, 2-(7,8-dihydro-1,6-naphthyridin-6(5H)-yl)-6,7-dimethoxy-5-(2-pyrimidinyl)- (9CI) (CA INDEX NAME)



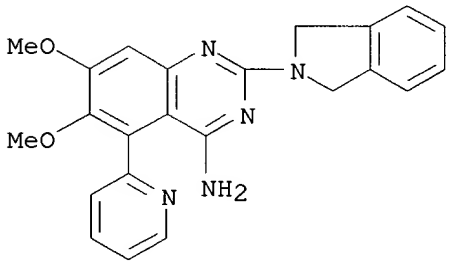
RN 210538-28-6 CAPLUS
CN 4-Quinazolinamine, 2-(7,8-dihydropyrido[4,3-d]pyrimidin-6(5H)-yl)-6,7-dimethoxy-5-(2-pyrimidinyl)- (9CI) (CA INDEX NAME)



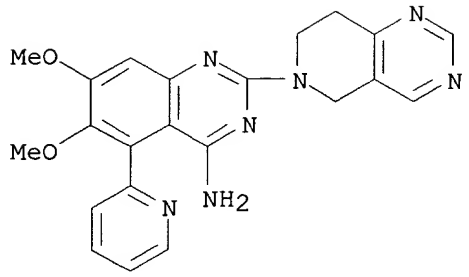
RN 210538-30-0 CAPLUS
CN 7-Isoquinolinesulfonamide, 2-[4-amino-6,7-dimethoxy-5-(2-pyridinyl)-2-quinazolinyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)



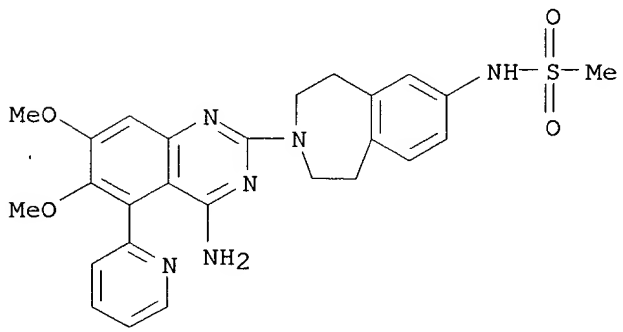
RN 210538-32-2 CAPLUS
CN 4-Quinazolinamine, 2-(1,3-dihydro-2H-isoindol-2-yl)-6,7-dimethoxy-5-(2-pyridinyl)- (9CI) (CA INDEX NAME)



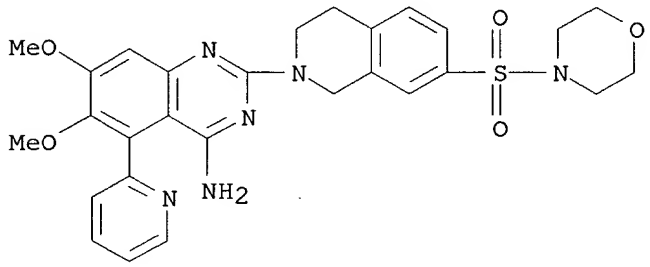
RN 210538-34-4 CAPLUS
CN 4-Quinazolinamine, 2-(7,8-dihydropyrido[4,3-d]pyrimidin-6(5H)-yl)-6,7-dimethoxy-5-(2-pyridinyl)- (9CI) (CA INDEX NAME)



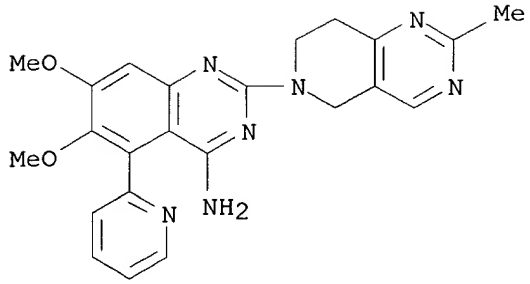
RN 210538-36-6 CAPLUS
CN Methanesulfonamide, N-[3-[4-amino-6,7-dimethoxy-5-(2-pyridinyl)-2-quinazolinyl]-2,3,4,5-tetrahydro-1H-3-benzazepin-7-yl]- (9CI) (CA INDEX NAME)



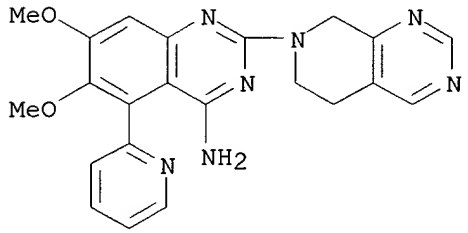
RN 210538-38-8 CAPLUS
CN Morpholine, 4-[[2-[4-amino-6,7-dimethoxy-5-(2-pyridinyl)-2-quinazolinyl]-1,2,3,4-tetrahydro-7-isoquinolinyl]sulfonyl]- (9CI) (CA INDEX NAME)



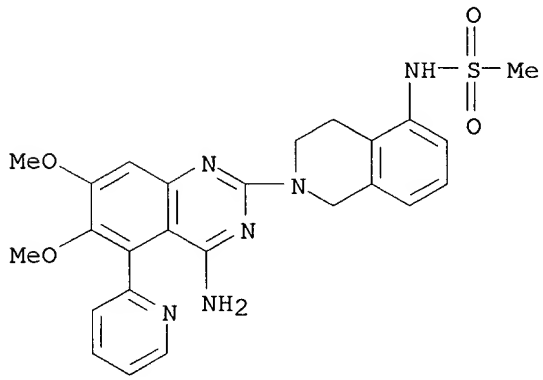
RN 210538-40-2 CAPLUS
CN 4-Quinazolinamine, 2-(7,8-dihydro-2-methylpyrido[4,3-d]pyrimidin-6(5H)-yl)-6,7-dimethoxy-5-(2-pyridinyl)- (9CI) (CA INDEX NAME)



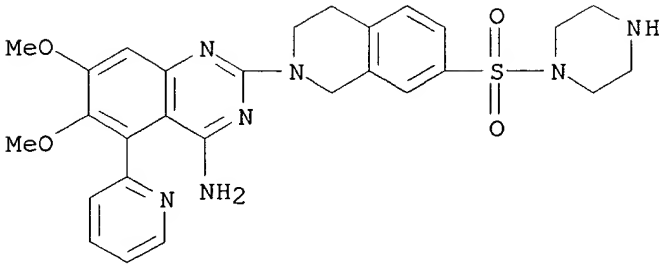
RN 210538-42-4 CAPLUS
CN 4-Quinazolinamine, 2-(5,8-dihydropyrido[3,4-d]pyrimidin-7(6H)-yl)-6,7-dimethoxy-5-(2-pyridinyl)- (9CI) (CA INDEX NAME)



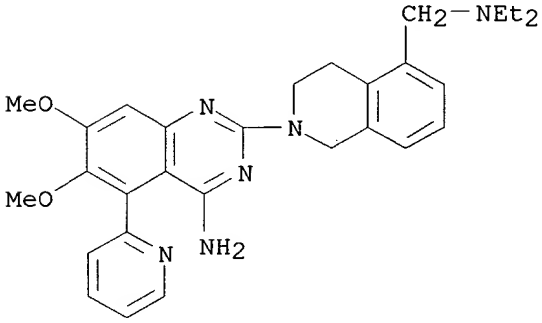
RN 210538-44-6 CAPLUS
CN Methanesulfonamide, N-[2-[4-amino-6,7-dimethoxy-5-(2-pyridinyl)-2-quinazolinyl]-1,2,3,4-tetrahydro-5-isoquinolinyl]- (9CI) (CA INDEX NAME)



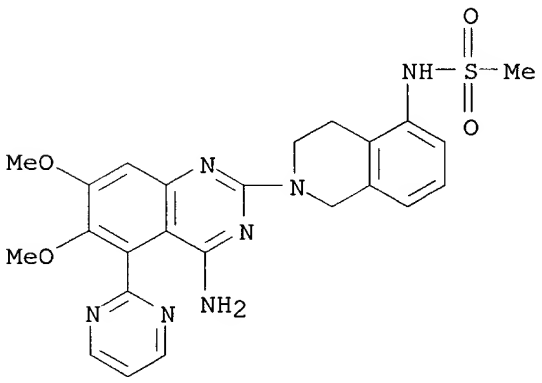
RN 210538-46-8 CAPLUS
CN Piperazine, 1-[[2-[4-amino-6,7-dimethoxy-5-(2-pyridinyl)-2-quinazolinyl]-1,2,3,4-tetrahydro-7-isoquinolinyl]sulfonyl]- (9CI) (CA INDEX NAME)



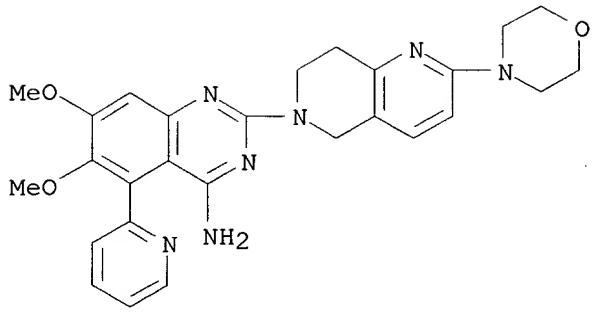
RN 210538-47-9 CAPLUS
CN 4-Quinazolinamine, 2-[5-[(diethylamino)methyl]-3,4-dihydro-2(1H)-isoquinolinyl]-6,7-dimethoxy-5-(2-pyridinyl)- (9CI) (CA INDEX NAME)



RN 210538-48-0 CAPLUS
CN Methanesulfonamide, N-[2-[4-amino-6,7-dimethoxy-5-(2-pyrimidinyl)-2-quinazolinyl]-1,2,3,4-tetrahydro-5-isoquinolinyl]- (9CI) (CA INDEX NAME)

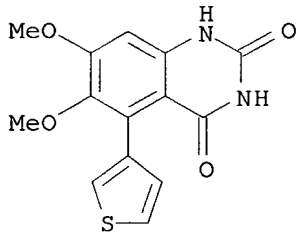


RN 210538-59-3 CAPLUS
CN 4-Quinazolinamine, 2-[7,8-dihydro-2-(4-morpholinyl)-1,6-naphthyridin-6(5H)-yl]-6,7-dimethoxy-5-(2-pyridinyl)- (9CI) (CA INDEX NAME)

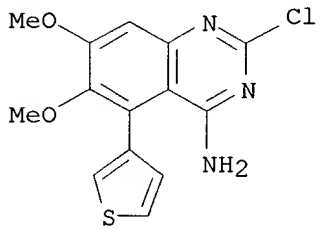


IT **210538-64-0P 210538-65-1P 210538-70-8P**
210538-77-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of quinoline and quinazoline derivs. useful in treatment of benign prostatic hyperplasia)

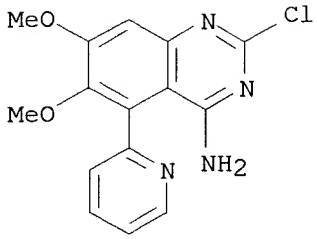
RN 210538-64-0 CAPLUS
CN 2,4(1H,3H)-Quinazolinedione, 6,7-dimethoxy-5-(3-thienyl)- (9CI) (CA INDEX NAME)



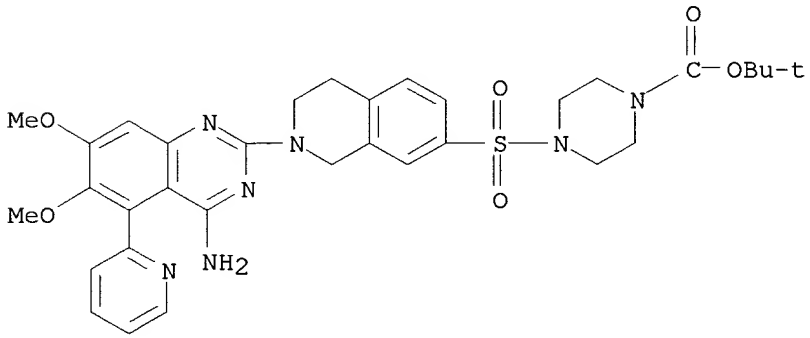
RN 210538-65-1 CAPLUS
CN 4-Quinazolinamine, 2-chloro-6,7-dimethoxy-5-(3-thienyl)- (9CI) (CA INDEX NAME)



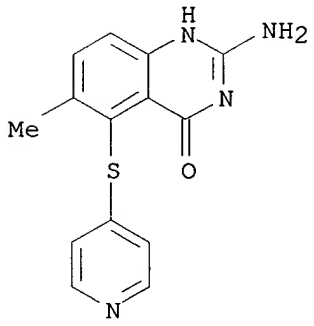
RN 210538-70-8 CAPLUS
CN 4-Quinazolinamine, 2-chloro-6,7-dimethoxy-5-(2-pyridinyl)- (9CI) (CA INDEX NAME)



RN 210538-77-5 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[2-[4-amino-6,7-dimethoxy-5-(2-pyridinyl)-2-quinazolinyl]-1,2,3,4-tetrahydro-7-isoquinolinyl]sulfonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

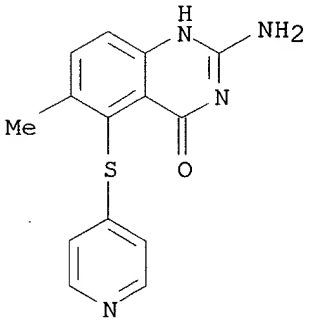


L14 ANSWER 13 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1998:224622 CAPLUS
DN 128:292952
TI Thymidylate biosynthesis in Trichinella spiralis development
AU Dabrowska, M.; Zielinski, Z.; Golos, B.; Michalski, R.; Rode, W.; Wranicz, M.; Pawelczak, K.
CS Nencki Institute of Experimental Biology, Academy of Sciences, Warsaw, Pol.
SO Chemistry and Biology of Pteridines and Folates 1997, Proceedings of the International Symposium on Pteridines and Folates, 11th, Berchtesgaden, Germany, June 15-20, 1997 (1997), 393-398. Editor(s): Pfleiderer, Wolfgang; Rokos, Hartmut. Publisher: Blackwell Wissenschafts-Verlag GmbH, Berlin, Germany.
CODEN: 65VBAF
DT Conference
LA English
AB In seeking a target in treatment of trichinellosis, Trichinella spiralis thymidylate synthesis, developmental pattern and properties of thymidylate synthase (TS; EC 2.1.1.45), a target in treatment, were studied.
IT **152946-68-4**, AG337
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(thymidylate biosynthesis in Trichinella spiralis development)
RN 152946-68-4 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)



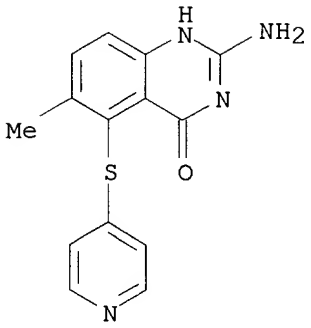
●2 HCl

L14 ANSWER 14 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1998:224592 CAPLUS
DN 128:289889
TI Combination studies of antifolates with 5-fluorouracil in colon cancer cell lines
AU Van Der Wilt, C. L.; Kuiper, C. M.; Pinedo, H. M.; Peters, G. J.
CS Dept. Medical Oncology, Academic Hospital Vrije Universiteit, Amsterdam, 1007 MB, Neth.
SO Chemistry and Biology of Pteridines and Folates 1997, Proceedings of the International Symposium on Pteridines and Folates, 11th, Berchtesgaden, Germany, June 15-20, 1997 (1997), 245-248. Editor(s): Pfleiderer, Wolfgang; Rokos, Hartmut. Publisher: Blackwell Wissenschafts-Verlag GmbH, Berlin, Germany.
CODEN: 65VBAF
DT Conference
LA English
AB The antiproliferative effects of 5-fluorouracil in combination with antifolates in colon cancer cell lines were mainly additive or close to additive.
IT **152946-68-4**, AG337
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination studies of antifolates with 5-fluorouracil in colon cancer cell lines)
RN 152946-68-4 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)



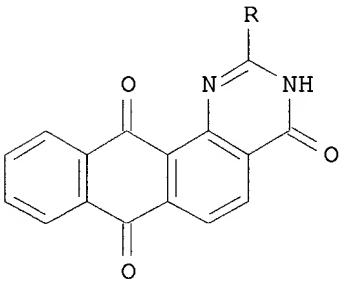
●2 HCl

L14 ANSWER 15 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1998:224588 CAPLUS
DN 129:144636
TI Role of cell culture medium folate levels on growth inhibition by thymidylate synthase inhibitors in squamous cell cancer and colon cancer cell lines
AU Backus, H. H. J.; Wouters, D.; Van Der Wilt, C. L.; Jansen, G.; Kuiper, C. M.; Van Groeningen, C. J.; Pinedo, H. M.; Peters, G. J.
CS Dept. Medical Oncology, University Hospital Vrije Universiteit, Amsterdam, 1007 MB, Neth.
SO Chemistry and Biology of Pteridines and Folates 1997, Proceedings of the International Symposium on Pteridines and Folates, 11th, Berchtesgaden, Germany, June 15-20, 1997 (1997), 229-232. Editor(s): Pfleiderer, Wolfgang; Rokos, Hartmut. Publisher: Blackwell Wissenschafts-Verlag GmbH, Berlin, Germany.
CODEN: 65VBAF
DT Conference
LA English
AB Cancer cell lines grown at low-folate conditions are more sensitive to antifolates the cell lines grown under std. conditions. Cells in folate-conditioned medium have a higher FPGS and RFC activity than cell lines cultured in std. folate culture medium. ZD 1694 is very cytotoxic in WiDr-F and C26-10-F that have a higher FPGS and RFC level. AG 337 inhibits thymidylate synthase independently of RFC and FPGS activity. There is no significant difference in sensitivity to AG 337 between colon cancer cell lines adapted to std. folate medium and folate-conditioned cell lines. There are much less difference in sensitivity to antifolates, FPGS and RFC transport activity between low-folate adapted SCC cell lines and SCC cell lines grown at std. folate levels. It seems likely that in SCC cell lines more factors are involved in the process.
IT **152946-68-4**, AG 337
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(role of cell culture medium folate levels on growth inhibition by thymidylate synthase inhibitors in squamous cell cancer and colon cancer cell lines)
RN 152946-68-4 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)

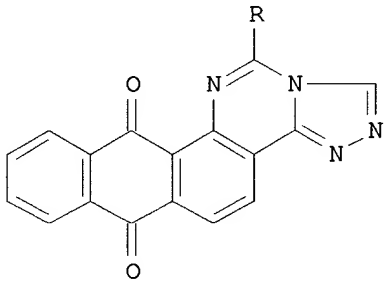


●2 HCl

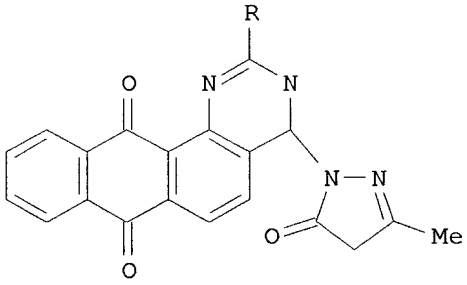
L14 ANSWER 16 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1998:68033 CAPLUS
DN 128:180382
TI Studies in anthraquinone: preparation of 2-substituted pyrimidoanthraquinones and related fused 1,2,4-triazolo, tetrazolo and pyrazolino derivatives
AU Kangani, C. O.; Master, H. E.
CS Nadkarny-Sacasa Research Laboratory, St. Xavier's College, Bombay, 400001, India
SO Journal of Heterocyclic Chemistry (1997), 34(6), 1699-1704
CODEN: JHTCAD; ISSN: 0022-152X
PB HeteroCorporation
DT Journal
LA English
GI



I

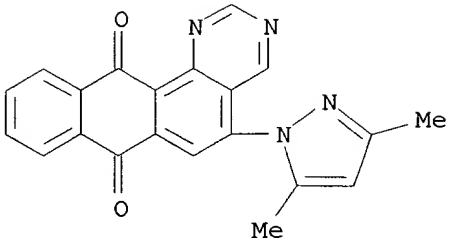


II

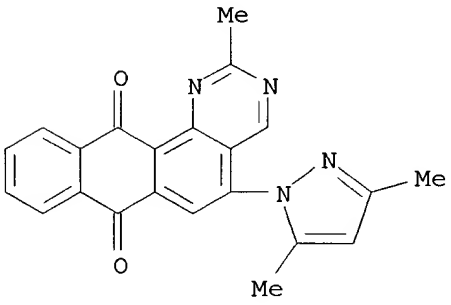


III

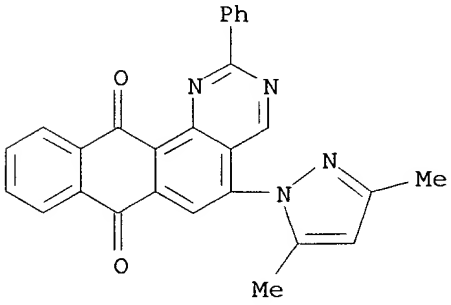
AB This paper describes the synthesis of 2-substituted-4(3H)-oxopyrimido[4,5-a]anthraquinone, e.g., I (R = H, Me, Ph), the corresponding 2-substituted-4-hydrazinopyrimido[4,5-a]anthraquinones, several 2-substituted-1,2,4-triazolo[4,3-c]pyrimido[4,5-a]-anthraquinones, e.g., II, tetrazolo[4,5-c]pyrimido[4,5-a]anthraquinones, and pyrazolinopyrimidoanthraquinone derivs.
IT **203126-54-9P 203126-55-0P 203126-56-1P**
203126-57-2P 203126-58-3P 203126-59-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of pyrimido-, fused triazolo-, tetrazolo-, and pyrazolino-anthraquinones)
RN 203126-54-9 CAPLUS
CN Naphtho[2,3-h]quinazoline-7,12-dione, 5-(3,5-dimethyl-1H-pyrazol-1-yl)- (9CI) (CA INDEX NAME)



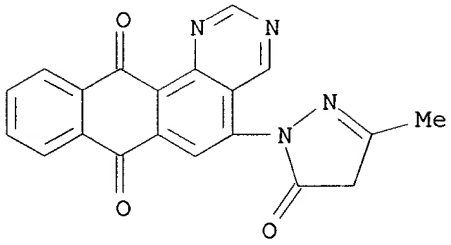
RN 203126-55-0 CAPLUS
CN Naphtho[2,3-h]quinazoline-7,12-dione, 5-(3,5-dimethyl-1H-pyrazol-1-yl)-2-methyl- (9CI) (CA INDEX NAME)



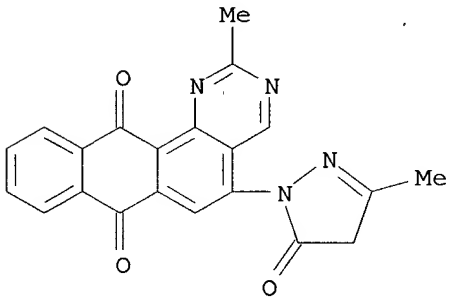
RN 203126-56-1 CAPLUS
CN Naphtho[2,3-h]quinazoline-7,12-dione, 5-(3,5-dimethyl-1H-pyrazol-1-yl)-2-phenyl- (9CI) (CA INDEX NAME)



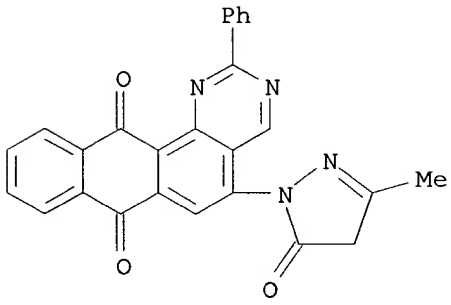
RN 203126-57-2 CAPLUS
CN Naphtho[2,3-h]quinazoline-7,12-dione, 5-(4,5-dihydro-3-methyl-5-oxo-1H-pyrazol-1-yl)- (9CI) (CA INDEX NAME)



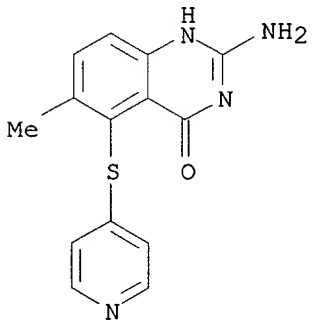
RN 203126-58-3 CAPLUS
CN Naphtho[2,3-h]quinazoline-7,12-dione, 5-(4,5-dihydro-3-methyl-5-oxo-1H-pyrazol-1-yl)-2-methyl- (9CI) (CA INDEX NAME)



RN 203126-59-4 CAPLUS
CN Naphtho[2,3-h]quinazoline-7,12-dione, 5-(4,5-dihydro-3-methyl-5-oxo-1H-pyrazol-1-yl)-2-phenyl- (9CI) (CA INDEX NAME)

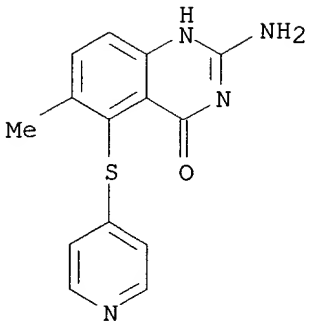


L4 ANSWER 17 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1998:49653 CAPLUS
DN 128:162467
TI Antifolates in clinical development
AU Takimoto, Chris H.
CS Developmental Therapeutics Department, Division of Clinical Sciences, National Cancer Institute, Medicine Branch, Bethesda Naval Hospital, Bethesda, MD, 20889-5105, USA
SO Seminars in Oncology (1997), 24(5, Suppl. 18), S18/40-S18/51
CODEN: SOLGAV; ISSN: 0093-7754
PB W. B. Saunders Co.
DT Journal; General Review
LA English
AB A review with 134 refs. Many novel antifolate compds. with unique pharmacol. properties are currently in clin. development. These newer antifolates differ from methotrexate, the most widely used and studied drug in this class, in terms of their lipid soly. and cellular transport affinity, their level of polyglutamation, and their specificity for inhibiting folate-dependent enzymes, such as dihydrofolate reductase, thymidylate synthase, or glycinamide ribonucleotide formyltransferase. The current status (i.e., mechanism of action, clin. response rates, and toxicity) of some of the newer antifolate compds. presently in clin. testing, including edatrexate, piritrexim, raltritrexed, LY 231514, AG337, AG331, 1843U89, ZD 9331, and lometrexol, is reviewed.
IT **152946-68-4**, AG 337
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(clin. pharmacol. of)
RN 152946-68-4 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)



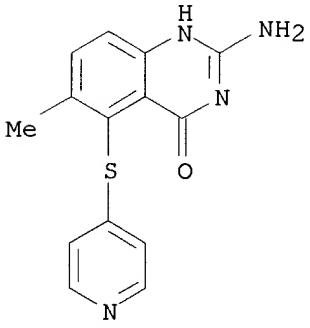
●2 HCl

L14 ANSWER 18 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1998:43350 CAPLUS
DN 128:162621
TI The relationship between intrinsic thymidylate synthase expression and sensitivity to THYMITAQ in human leukemia and colorectal carcinoma cell lines
AU Estlin, E. J.; Balmanno, K.; Calvert, A. H.; Hall, A. G.; Lunec, J.; Newell, D. R.; Pearson, A. D. J.; Taylor, G. A.
CS Dep. of Paediatric Oncology, Royal Victoria Infirmary, Sir James Spence Institute for Child Health, Newcastle upon Tyne, NE2 4LP, UK
SO British Journal of Cancer (1997), 76(12), 1579-1585
CODEN: BJCAAI; ISSN: 0007-0920
PB Churchill Livingstone
DT Journal
LA English
AB Thymidylate synthase (TS) expression has been characterized for a panel of eight human colorectal carcinoma and five human leukemia cell lines, to relate differences in intrinsic TS activity, protein and mRNA levels to growth inhibition caused by continuous exposure to THYMITAQ, a specific non-classical antifolate TS inhibitor. Although a 20-fold variation in sensitivity to THYMITAQ was found within the colorectal cell line panel (IC50 0.12-2.7 .mu.M), sensitivity was not related to TS activity, TS protein or TS mRNA levels. For the leukemic cell lines, only a twofold range in sensitivity to THYMITAQ was obsd. (IC50 0.87-2.3 .mu.M), and this did not correlate with TS activity, TS protein or TS mRNA levels. Across all of the cell lines, TS activity was linearly related to TS protein levels ($r2 = 0.87$, $P < 0.0001$). However, for both the colorectal and leukemia cell line panels, no relationship was found between TS mRNA/18S rRNA ratios and either TS activity or TS protein, consistent with the importance of post-transcriptional mechanisms in regulating TS activity. Two of the colorectal cell lines (BE and HCT116) and one of the human leukemic cell lines (HL60), were intrinsically resistant to THYMITAQ (IC50 < 2 .mu.m) in the absence of TS overexpression, suggesting that, subsequent to TS inhibition, events such as DNA repair and tolerance to apoptotic stimuli are also important determinants of sensitivity to THYMITAQ.
IT **152946-68-4**, THYMITAQ
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(the relationship between intrinsic thymidylate synthase expression and sensitivity to THYMITAQ in human leukemia and colorectal carcinoma cell lines)
RN 152946-68-4 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)



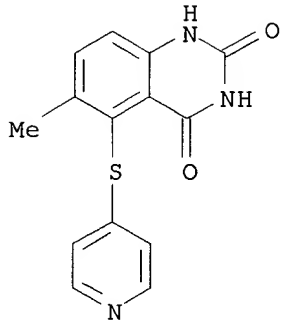
●2 HCl

L14 ANSWER 19 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1997:773231 CAPLUS
DN 128:97399
TI Antitumor activity of oxaliplatin in combination with 5-fluorouracil and the thymidylate synthase inhibitor AG337 in human colon, breast and ovarian cancers
AU Raymond, E.; Buquet-Fagot, C.; Djelloul, S.; Mester, J.; Cvitkovic, E.; Allain, P.; Louvet, C.; Gespach, C.
CS INSERM U55, IFR 65, Hop. Saint-Antoine, Paris, 75571, Fr.
SO Anti-Cancer Drugs (1997), 8(9), 876-885
CODEN: ANTDEV; ISSN: 0959-4973
PB Rapid Science Publishers
DT Journal
LA English
AB Oxaliplatin, classical [5-fluorouracil (5-FU)] and non-classical (AG337) thymidylate synthase inhibitors have shown promising activity in the treatment of cancer. This study investigates the cytotoxic effects of oxaliplatin in combination with 5-FU and AG337 in cultured human colon (HT29, CaCo2), breast(MCF-7, MDA-MB-231) and ovarian (2008) cancer cell lines, and their derived counterparts selected for their resistance to 5-FU (HT29-5-FU), doxorubicin (MCF-7mdr) or cisplatin (2008C13). Therapeutic expts. were conducted in mice bearing colon-HT29 xenografts and in the GR hormone-independent mammary carcinoma model. In vitro, oxaliplatin shows potent cytotoxic activity in colon (IC50 from 2.1 to 5.9 .mu.M), ovarian (IC50 = 10 .mu.M) and breast cancer cells (IC50 from 7.4 to 17.9 .mu.M). Oxaliplatin was a potent inhibitor of DNA synthesis and bound to cellular DNA. Surprisingly, the overall amt. of oxaliplatin DNA binding was significantly inferior to that induced by isocytotoxic concns. of cisplatin in HT29. In vitro, synergistic antiproliferative effects were obsd. when oxaliplatin was added to 5-FU and AG337. Those synergistic effects of combinations were maintained in colon HT29-5-FU cancer cells. In vivo, 5-FU increased significantly the antitumor activity of oxaliplatin in HT29 xenografts, and similarly 5-FU and AG337 increased the activity of oxaliplatin in the GR tumor model. These data may encourage further clin. investigation of oxaliplatin in combination with classical and non-classical thymidylate synthase inhibitors in the treatment of human cancers.
IT **152946-68-4**, AG337
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergistic antitumor activity of oxaliplatin, 5-fluorouracil and AG337 in human colon, breast and ovarian cancers)
RN 152946-68-4 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)



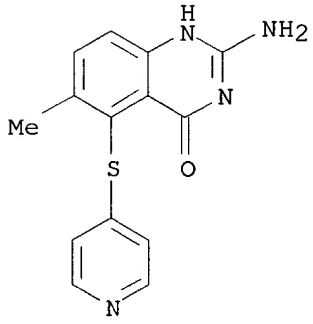
●2 HCl

L14 ANSWER 20 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1997:737651 CAPLUS
DN 128:16381
TI Preformulation studies for the development of a parenteral liquid formulation of an antitumor agent, AG337
AU Li, Shihong; Zamansky, Irina; Orlov, Irina; Tyle, Praveen; Roy, Samir D.
CS Agouron Pharmaceuticals, Incorporated, La Jolla, CA, 92037, USA
SO PDA Journal of Pharmaceutical Science and Technology (1997), 51(5), 181-186
CODEN: JPHTEU; ISSN: 1076-397X
PB PDA, Inc.
DT Journal
LA English
AB AG337 is a potential anticancer agent designed by using protein structure-based techniques. The objective of this work was to evaluate the feasibility of a high concn. liq. formulation of AG337 intended for i.v. administration. The soly. of AG337 in pure water was >100 mg/mL at pH <3. The drug soly. decreased precipitously as the soln. pH increased above 3 upon titrn. with 0.1N NaOH. The soly. of AG337 in water as a function of temp. (ranging from 2-40.degree.) was detd. As anticipated, the drug soly. increased somewhat linearly as the soln. temp. increased. Degrdn. kinetics of 15 and 10% AG337 solns. at elevated temps. was detd. to assess the feasibility of a liq. formulation as opposed to previously developed lyophilized powder for injection. Only 1 major degrdn. product was detected in the HPLC as a result of chem. hydrolysis of AG337 to AG408. Arrhenius plot (i.e., kobs vs. I/T) revealed an activation energy of 25 kcal/mol. The shelf-life (t95%) of 10% AG337 soln. of pH 2 at 25.degree. was predicted to be roughly 8 yr. Various terminal sterilization methods, which include moist/dry autoclaving (121.degree.), electron beam, and .gamma.-irradn., were evaluated for the 10% AG337 soln. Autoclaving cycles, ranged from 20 to 90 min, caused instantaneous degrdn. of AG337 soln. and induced further degrdn. upon long-term storage. Again, AG408 was the major degrdn. product following autoclaving. On the other hand, irradn. techniques induced very little degrdn., but turned clear glass vials to brown upon irradn.
IT **199182-73-5**, AG 408
RL: FMU (Formation, unclassified); PRP (Properties); FORM (Formation, nonpreparative)
(preformulation studies for parenteral liq. formulation AG337)
RN 199182-73-5 CAPLUS
CN 2,4(1H,3H)-Quinazolinedione, 6-methyl-5-(4-pyridinylthio)-, monohydrochloride (9CI) (CA INDEX NAME)



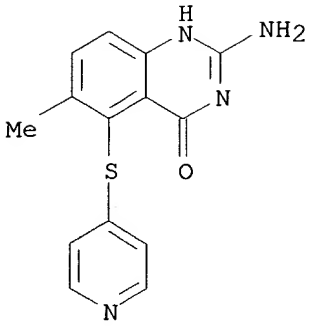
● HCl

IT **152946-68-4,** AG337
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preformulation studies for parenteral liq. formulation AG337)
RN 152946-68-4 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 21 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1997:514953 CAPLUS
DN 127:214683
TI Cross-resistance to antifolates in multidrug resistant cell lines with P-glycoprotein or multidrug resistance protein expression
AU Van Triest, Baukelien; Pinedo, Herbert M.; Telleman, Frank; Van Der Wilt, Clasina L.; Jansen, Gerrit; Peters, Godefridus J.
CS DEPARTMENT OF MEDICAL ONCOLOGY, UNIVERSITY HOSPITAL VRIJE UNIVERSITEIT, AMSTERDAM, 1007 MB, Neth.
SO Biochemical Pharmacology (1997), 53(12), 1855-1866
CODEN: BCPCA6; ISSN: 0006-2952
PB Elsevier
DT Journal
LA English
AB Resistance to some (lipophilic) antifolates has been assocd. with P-glycoprotein (P-gp)-mediated multidrug resistance (MDR). A possible relation with non-P-gp MDR has not been established. We studied resistance to antifolates in SW-1573 human lung carcinoma cells, a P-gp overexpressing variant SW-1573/2R160 and a multidrug resistance protein (MRP) overexpressing variant SW-1573/2R120. In this study, thymidylate synthase (TS) inhibitors with different properties concerning the efficiency of membrane transport and the efficiency of polyglutamylation were tested for cross-resistance in SW-1573/2R120 and SW-1573/2R160 cells. Growth inhibition patterns in this cell line panel were measured by the Sulforhodamine B (SRB) assay. Resistance factors for TS inhibitors were: 2.4 and 0.4 for 5-fluorouracil (5FU), 18.8 and 8.8 for ZD1694, 17 and 0.7 for AG337, and 40 and 8.3 for BW1843U89 in SW-1573/2R160 and SW-1573/2R120, resp. This study showed changes in the TS enzyme kinetics during the induction of doxorubicin resistance in both SW-1573 variants, resulting in 2-fold lower Km values for 2'-deoxyuridine-5'-monophosphate (dUMP) in both resistant variants compared to the parental cell line. TS activity, TS protein induction and TS mRNA expression all had 2-fold increased in the SW-1573/2R120 compared to the SW-1573/2R160. 3H-MTX influx was 2-fold lower in SW-1573/2R160 cells compared to SW-1573/2R120 and SW-1573 cells. In the SW-1573/2R160 cell line, an aberrant intracellular trafficking towards the target TS was obsd., compared to SW-1573/2R120 and SW-1573 cells as measured by the TS in situ assay. The rate of TS inhibition by the TS inhibitors used in this study was similar in all cell lines. In conclusion, collateral sensitivity to 5FU and the lipophilic AG337 and cross-resistance to other antifolates were obsd. in non-P-gp MDR SW-1573/2R120 cells, as well as resistance to all antifolates in P-gp SW-1573/2R160 cells. The mechanism of resistance in SW-1573/2R160 cells possibly involves reduced influx and changes in intracellular trafficking routes. For the SW-1573/2R120 cell line, several changes related to the TS enzyme possibly play a role in the obsd. cross-resistance and collateral sensitivity pattern.
IT **152946-68-4**, AG337
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cross-resistance to antifolates in multidrug resistant cell lines with P-glycoprotein or multidrug resistance protein expression)
RN 152946-68-4 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 22 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1997:506728 CAPLUS
DN 127:121749
TI Preparation of quinolines and quinazolines for treatment of benign prostatic hyperplasia
IN Collis, Alan John; Fox, David Nathan Abraham; Newman, Julie
PA Pfizer Research and Development Company, N.V./S.A, UK; Pfizer Inc.; Collis, Alan John; Fox, David Nathan Abraham; Newman, Julie
SO PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

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	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9713719	A1	19970717	AU 1997-13719	19961205
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PRAI	GB 1995-26546	A	19951223		
	WO 1996-EP5609	W	19961205		
	US 2000-613500	B1	20000710		

OS MARPAT 127:121749
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; R1 = C1-4 alkoxy optically substituted by one or more F atoms; R2 = H, C1-6 alkoxy optionally substituted by one or more F atoms; R3 = H, halo, C1-4 alkoxy, CF3; R2R3 = OCH2, the methylene group being attached to the ortho-position of the pendant Ph ring; R4 = 4-6-membered heterocyclic ring contg. 1-2 heteroatoms selected from N, O and S, the ring being optionally fused to a benzene ring, (un)substituted 5-6-membered heterocyclic ring contg. 1-2 heteroatoms selected from N, O and S; X = CH, N; L = a bond, II (wherein N is attached to the 2-position of the quinoline or quinazoline ring; A = a bond, CO, SO2; Z = CH, N; m = 0-2; n = 1-3), N(R6)(CH2)pZ'(R7)A' (wherein N is attached to the 2-position of the quinoline or quinazoline ring; A', Z' = A, Z; R6, R7 =

H, C1-4 alkyl; p = 0-3)], useful in the treatment of inter alia benign prostatic hyperplasia, were prepd. Thus, reacting N-benzyl-3S,4S-bis(tert-butyldimethylsilyloxy)pyrrolidine with phosgene in PhMe followed by treatment of the intermediate with homopiperazine in THF, and reaction of the resulting 1-{1-[3S,4S-bis(tert-butyldimethylsilyloxy)pyrrolidine]carbonyl}-1,4-diazepane with 4-amino-2-chloro-6,7-dimethoxy-5-phenylquinazoline in the presence of Et3N in n-BuOH afforded (3S,4S)-III.HCl which showed pA2 of 8.5.

IT **192868-61-4P 192868-62-5P 192868-63-6P**
192868-64-7P 192868-65-8P 192868-66-9P
192868-69-2P 192868-70-5P 192868-71-6P
192868-75-0P 192868-76-1P 192868-77-2P
192868-78-3P 192868-79-4P 192868-80-7P
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192868-84-1P 192868-85-2P 192868-86-3P
192868-87-4P 192868-88-5P 192868-89-6P
192868-90-9P 192868-91-0P 192868-92-1P
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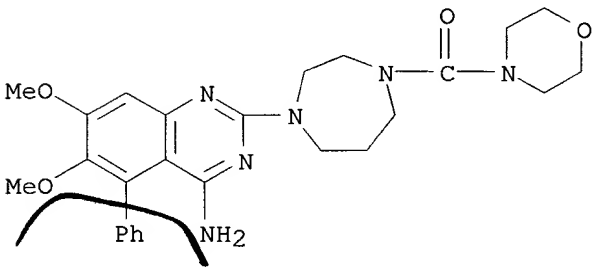
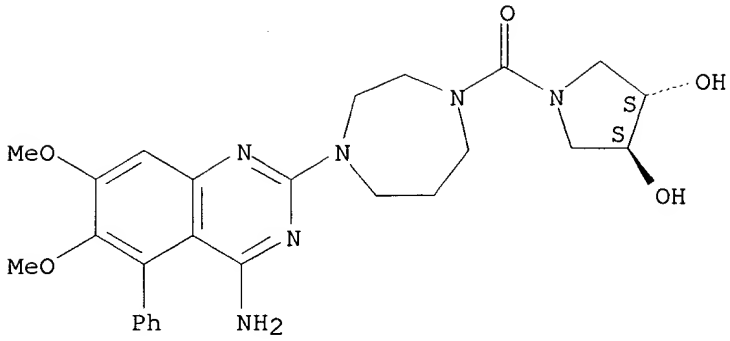
192868-99-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of quinolines and quinazolines for treatment of benign prostatic hyperplasia)

RN 192868-61-4 CAPLUS
CN 1H-1,4-Diazepine, 1-(4-amino-6,7-dimethoxy-5-phenyl-2-quinazolinyl)hexahydro-4-(4-morpholinylcarbonyl)- (9CI) (CA INDEX NAME)



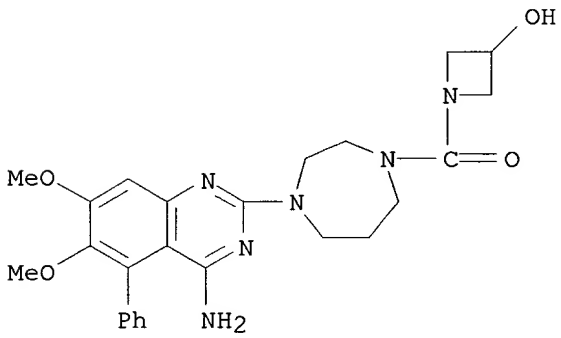
RN 192868-62-5 CAPLUS
CN 1H-1,4-Diazepine, 1-(4-amino-6,7-dimethoxy-5-phenyl-2-quinazolinyl)-4-[(3,4-dihydroxy-1-pyrrolidinyl)carbonyl]hexahydro-, monohydrochloride, (3S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



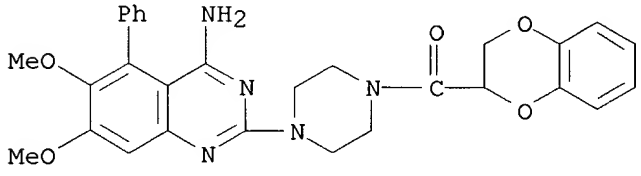
● HCl

RN 192868-63-6 CAPLUS
CN 1H-1,4-Diazepine, 1-(4-amino-6,7-dimethoxy-5-phenyl-2-quinazolinyl)hexahydro-4-[(3-hydroxy-1-azetidinyl)carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)



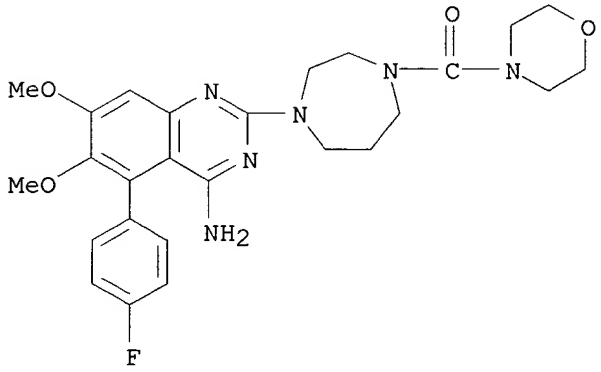
● HCl

RN 192868-64-7 CAPLUS
CN Piperazine, 1-(4-amino-6,7-dimethoxy-5-phenyl-2-quinazolinyl)-4-[(2,3-dihydro-1,4-benzodioxin-2-yl)carbonyl]- (9CI) (CA INDEX NAME)

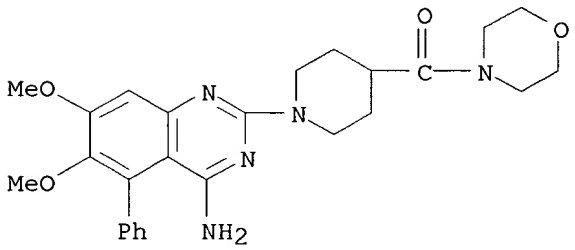


RN 192868-65-8 CAPLUS
CN 1H-1,4-Diazepine, 1-[4-amino-5-(4-fluorophenyl)-6,7-dimethoxy-2-

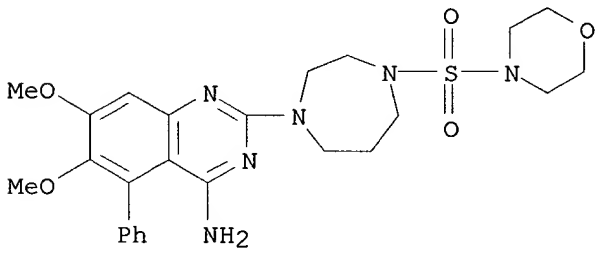
quinazolinyl]hexahydro-4-(4-morpholinylcarbonyl)- (9CI) (CA INDEX NAME)



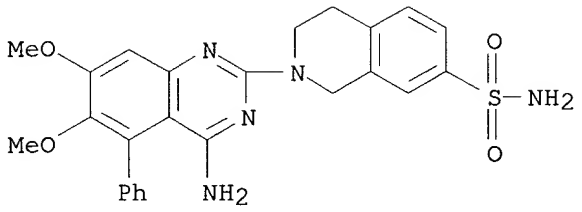
RN 192868-66-9 CAPLUS
CN Morpholine, 4-[[1-(4-amino-6,7-dimethoxy-5-phenyl-2-quinazolinyl)-4-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)



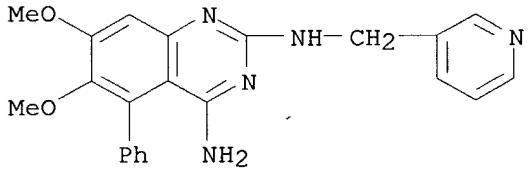
RN 192868-69-2 CAPLUS
CN 1H-1,4-Diazepine, 1-(4-amino-6,7-dimethoxy-5-phenyl-2-quinazolinyl)hexahydro-4-(4-morpholinylsulfonyl)- (9CI) (CA INDEX NAME)



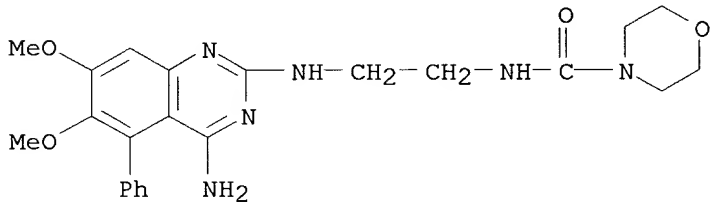
RN 192868-70-5 CAPLUS
CN 7-Isoquinolinesulfonamide, 2-(4-amino-6,7-dimethoxy-5-phenyl-2-quinazolinyl)-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)



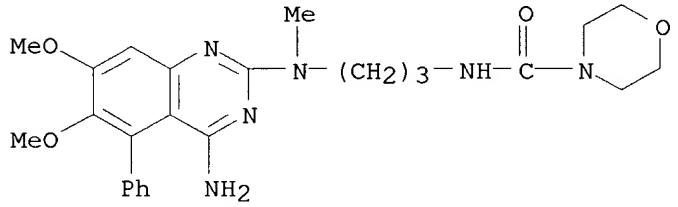
RN 192868-71-6 CAPLUS
CN 2,4-Quinazolinediamine, 6,7-dimethoxy-5-phenyl-N2-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



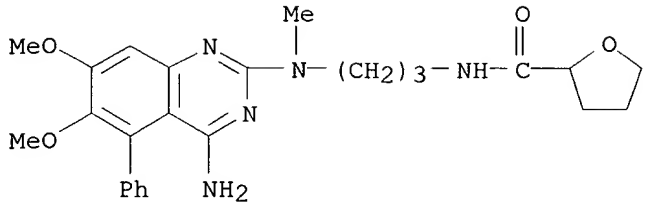
RN 192868-75-0 CAPLUS
CN 4-Morpholinecarboxamide, N-[2-[(4-amino-6,7-dimethoxy-5-phenyl-2-quinazolinyl)amino]ethyl]- (9CI) (CA INDEX NAME)



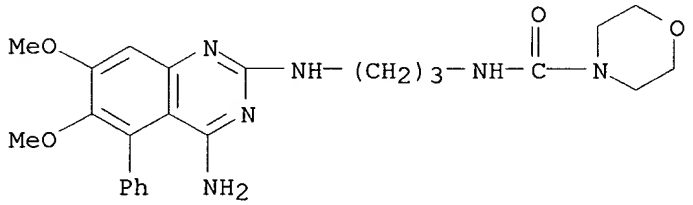
RN 192868-76-1 CAPLUS
CN 4-Morpholinecarboxamide, N-[3-[(4-amino-6,7-dimethoxy-5-phenyl-2-quinazolinyl)methylamino]propyl]- (9CI) (CA INDEX NAME)



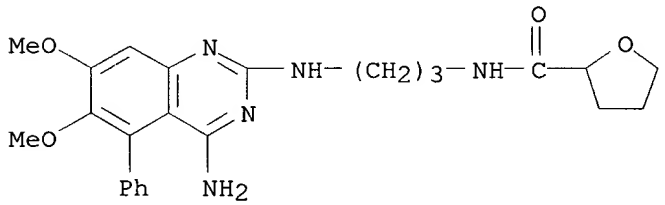
RN 192868-77-2 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-5-phenyl-2-quinazolinyl)methylamino]propyl]tetrahydro- (9CI) (CA INDEX NAME)



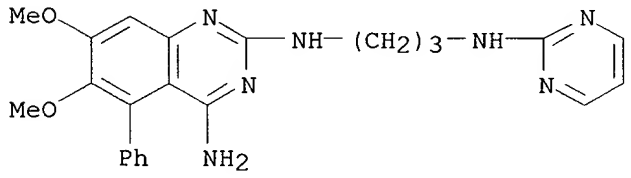
RN 192868-78-3 CAPLUS
CN 4-Morpholinecarboxamide, N-[3-[(4-amino-6,7-dimethoxy-5-phenyl-2-quinazolinyl)amino]propyl]- (9CI) (CA INDEX NAME)



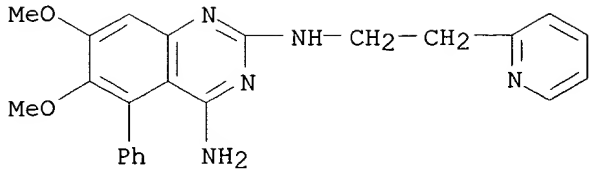
RN 192868-79-4 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-5-phenyl-2-quinazolinyl)amino]propyl]tetrahydro- (9CI) (CA INDEX NAME)



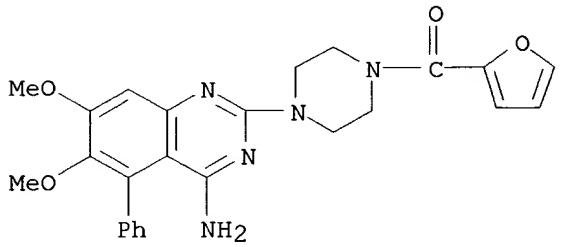
RN 192868-80-7 CAPLUS
CN 2,4-Quinazolinediamine, 6,7-dimethoxy-5-phenyl-N2-[3-(2-pyrimidinylamino)propyl]- (9CI) (CA INDEX NAME)



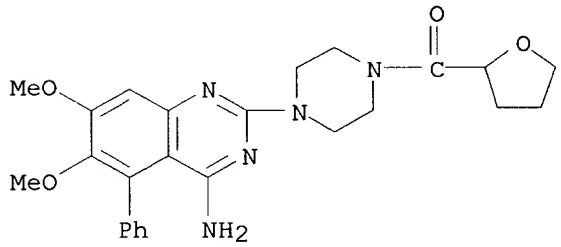
RN 192868-81-8 CAPLUS
CN 2,4-Quinazolinediamine, 6,7-dimethoxy-5-phenyl-N2-[2-(2-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)



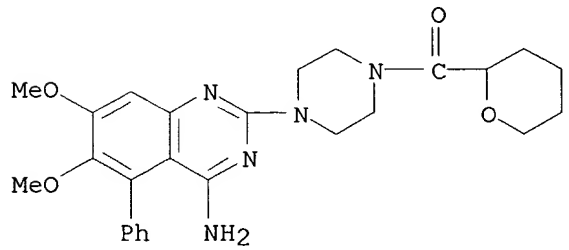
RN 192868-82-9 CAPLUS
CN Piperazine, 1-(4-amino-6,7-dimethoxy-5-phenyl-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



RN 192868-83-0 CAPLUS
CN Piperazine, 1-(4-amino-6,7-dimethoxy-5-phenyl-2-quinazolinyl)-4-[(tetrahydro-2-furanyl)carbonyl]- (9CI) (CA INDEX NAME)

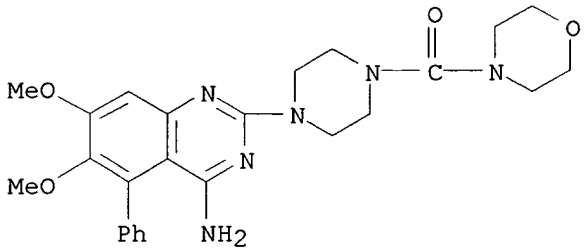


RN 192868-84-1 CAPLUS
CN Piperazine, 1-(4-amino-6,7-dimethoxy-5-phenyl-2-quinazolinyl)-4-[(tetrahydro-2H-pyran-2-yl)carbonyl]- (9CI) (CA INDEX NAME)

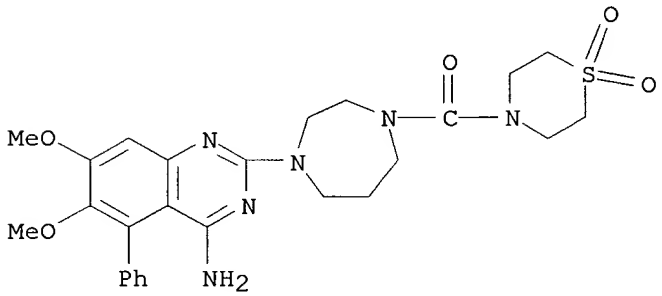


RN 192868-85-2 CAPLUS

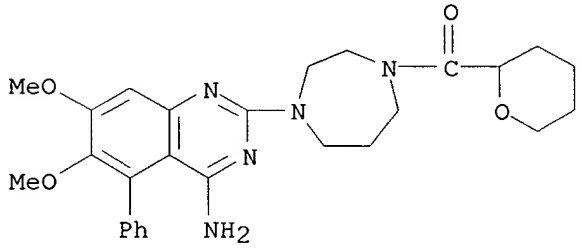
CN Morpholine, 4-[[4-(4-amino-6,7-dimethoxy-5-phenyl-2-quinazolinyl)-1-piperazinyl]carbonyl]- (9CI) (CA INDEX NAME)



RN 192868-86-3 CAPLUS
CN 1H-1,4-Diazepine, 1-(4-amino-6,7-dimethoxy-5-phenyl-2-quinazolinyl)-4-[(1,1-dioxido-4-thiomorpholinyl)carbonyl]hexahydro- (9CI) (CA INDEX NAME)

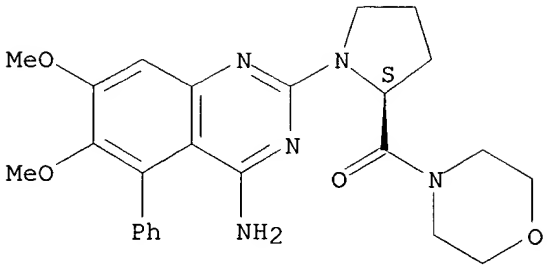


RN 192868-87-4 CAPLUS
CN 1H-1,4-Diazepine, 1-(4-amino-6,7-dimethoxy-5-phenyl-2-quinazolinyl)hexahydro-4-[(tetrahydro-2H-pyran-2-yl)carbonyl]- (9CI) (CA INDEX NAME)

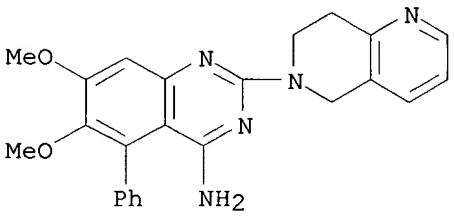


RN 192868-88-5 CAPLUS
CN Morpholine, 4-[[1-(4-amino-6,7-dimethoxy-5-phenyl-2-quinazolinyl)-2-pyrrolidinyl]carbonyl]-, (S)- (9CI) (CA INDEX NAME)

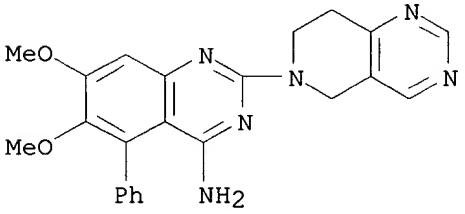
Absolute stereochemistry.



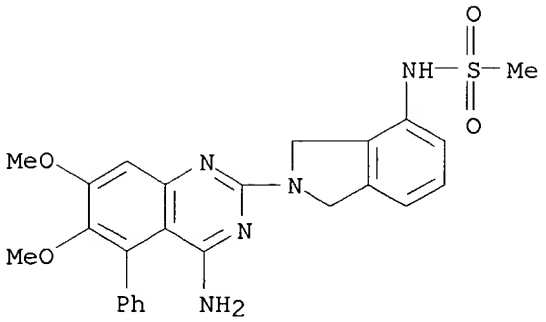
RN 192868-89-6 CAPLUS
CN 4-Quinazolinamine, 2-(7,8-dihydro-1,6-naphthyridin-6(5H)-yl)-6,7-dimethoxy-5-phenyl- (9CI) (CA INDEX NAME)



RN 192868-90-9 CAPLUS
CN 4-Quinazolinamine, 2-(7,8-dihydropyrido[4,3-d]pyrimidin-6(5H)-yl)-6,7-dimethoxy-5-phenyl- (9CI) (CA INDEX NAME)

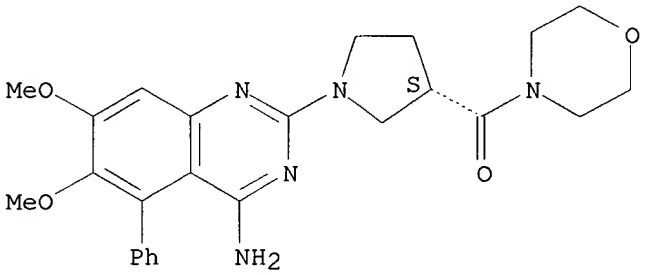


RN 192868-91-0 CAPLUS
CN Methanesulfonamide, N-[2-(4-amino-6,7-dimethoxy-5-phenyl-2-quinazolinyl)-2,3-dihydro-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

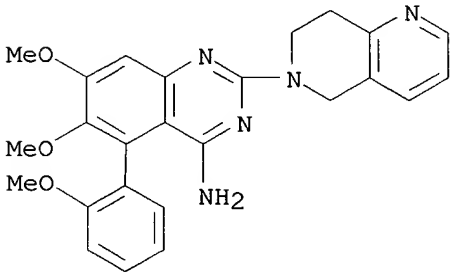


RN 192868-92-1 CAPLUS
CN Morpholine, 4-[[1-(4-amino-6,7-dimethoxy-5-phenyl-2-quinazolinyl)-3-pyrrolidinyl]carbonyl]-, (S)- (9CI) (CA INDEX NAME)

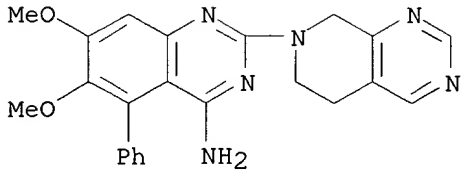
Absolute stereochemistry.



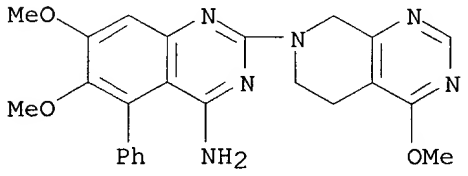
RN 192868-93-2 CAPLUS
CN 4-Quinazolinamine, 2-(7,8-dihydro-1,6-naphthyridin-6(5H)-yl)-6,7-dimethoxy-5-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



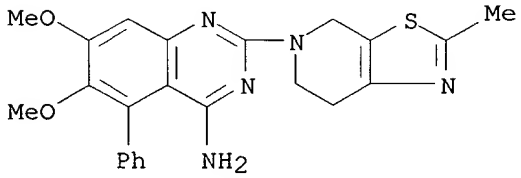
RN 192868-97-6 CAPLUS
CN 4-Quinazolinamine, 2-(5,8-dihydropyrido[3,4-d]pyrimidin-7(6H)-yl)-6,7-dimethoxy-5-phenyl- (9CI) (CA INDEX NAME)



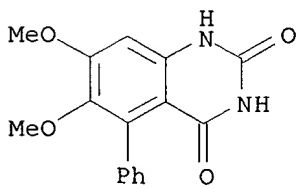
RN 192868-98-7 CAPLUS
CN 4-Quinazolinamine, 2-(5,8-dihydro-4-methoxypyrido[3,4-d]pyrimidin-7(6H)-yl)-6,7-dimethoxy-5-phenyl- (9CI) (CA INDEX NAME)



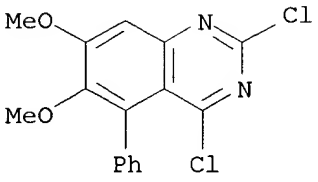
RN 192868-99-8 CAPLUS
CN 4-Quinazolinamine, 2-(6,7-dihydro-2-methylthiazolo[5,4-c]pyridin-5(4H)-yl)-6,7-dimethoxy-5-phenyl- (9CI) (CA INDEX NAME)



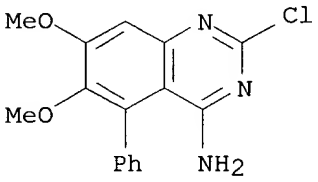
IT **192869-31-1P 192869-32-2P 192869-33-3P**
192869-34-4P 192869-36-6P 192869-44-6P
192869-45-7P 192869-46-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of quinolines and quinazolines for treatment of benign prostatic hyperplasia)
RN 192869-31-1 CAPLUS
CN 2,4(1H,3H)-Quinazolinedione, 6,7-dimethoxy-5-phenyl- (9CI) (CA INDEX NAME)



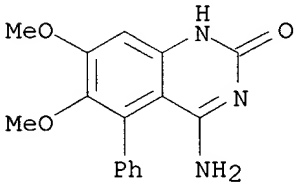
RN 192869-32-2 CAPLUS
CN Quinazoline, 2,4-dichloro-6,7-dimethoxy-5-phenyl- (9CI) (CA INDEX NAME)



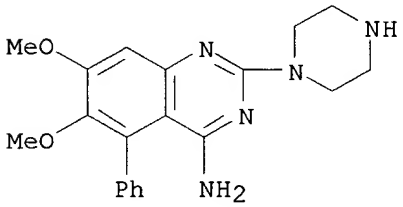
RN 192869-33-3 CAPLUS
CN 4-Quinazolinamine, 2-chloro-6,7-dimethoxy-5-phenyl- (9CI) (CA INDEX NAME)



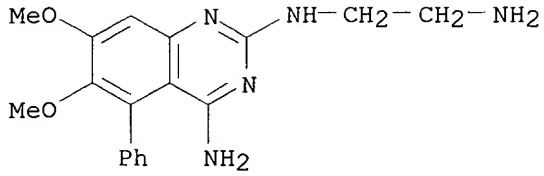
RN 192869-34-4 CAPLUS
CN 2(1H)-Quinazolinone, 4-amino-6,7-dimethoxy-5-phenyl- (9CI) (CA INDEX NAME)



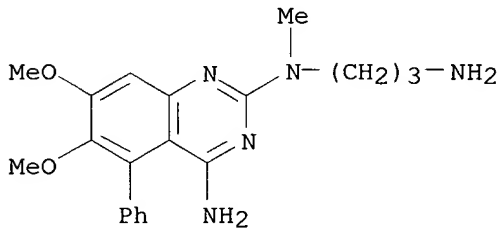
RN 192869-36-6 CAPLUS
CN 4-Quinazolinamine, 6,7-dimethoxy-5-phenyl-2-(1-piperazinyl)- (9CI) (CA INDEX NAME)



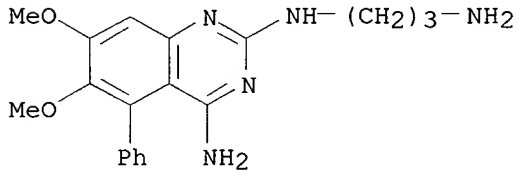
RN 192869-44-6 CAPLUS
CN 2,4-Quinazolinediamine, N2-(2-aminoethyl)-6,7-dimethoxy-5-phenyl- (9CI) (CA INDEX NAME)



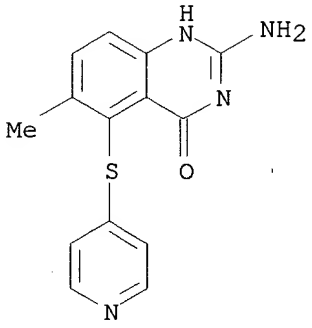
RN 192869-45-7 CAPLUS
CN 2,4-Quinazolinediamine, N2-(3-aminopropyl)-6,7-dimethoxy-N2-methyl-5-phenyl- (9CI) (CA INDEX NAME)



RN 192869-46-8 CAPLUS
CN 2,4-Quinazolinediamine, N2-(3-aminopropyl)-6,7-dimethoxy-5-phenyl- (9CI) (CA INDEX NAME)

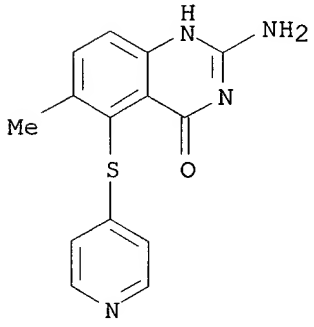


L14 ANSWER 23 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1997:427219 CAPLUS
DN 127:90258
TI Cellular pharmacology and in vivo activity of a new anticancer agent, ZD9331: a water-soluble, nonpolyglutamatable, quinazoline-based inhibitor of thymidylate synthase
AU Jackman, Ann L.; Kimbell, Rosemary; Aherne, G. Wynne; Brunton, Lisa; Jansen, Gerrit; Stephens, Trevor C.; Smith, Michael N.; Wardleworth, J. Michael; Boyle, F. Thomas
CS The Cancer Research Campaign Centre for Cancer Therapeutics at the Institute of Cancer Research, Surrey, SM2 5NG, UK
SO Clinical Cancer Research (1997), 3(6), 911-921
CODEN: CCREF4; ISSN: 1078-0432
PB American Association for Cancer Research
DT Journal
LA English
AB ZD9331 is a drug that was developed from a potent class of water-sol., C7-methyl-substituted, quinazoline-based inhibitors of thymidylate synthase (TS) that are transported into cells via a saturable, carrier-mediated system (reduced folate carrier, or RFC) but are not substrates for folylpolyglutamate synthetase. ZD9331 is the .gamma.-tetrazole analog of 2-desamino-2,7-dimethyl-N10-propargyl-2'-fluoro-5,8-dideazafolate (ZM214888), with a TS Ki of .apprx.0.4 nM. ZD9331 exhibits potent growth inhibitory and cytotoxic activity; e.g., IC50 for the inhibition of human W1L2 lymphoblastoid cell line was 7 nM. The addn. of thymidine to the culture medium increased the IC50 in W1L2 cells >10,000-fold, demonstrating the high specificity of the drug for TS. ZD9331 is transported into cells predominantly via the RFC. Accordingly, it competes with methotrexate (MTX) and folinic acid for cellular uptake and has reduced activity against two cell lines with low expression of the RFC (L1210:1565 and CEM/MTX). In addn., a cell line with acquired resistance to ZD9331 displays reduced uptake of both ZD9331 and MTX. A mouse cell line (L1210:RD1694), with acquired resistance to ZD1694 due to reduced folylpolyglutamate synthetase activity, was not significantly cross-resistant to ZD9331. The flux through TS, as measured by 3H release from 5-[3H]deoxyuridine, was rapidly inhibited when cells were incubated with ZD9331. However, because ZD9331 cannot form polyglutamates, TS activity recovered rapidly once cells were placed in drug-free medium. The min. curative dose of ZD9331 in the i.m. L5178Y TK-/- tumor model was .apprx.3 mg/kg when given by 24-h continuous infusion, and it was 25-50 mg/kg when given by a single i.p. or i.v. injection. ZD9331 had antitumor activity against the L5178Y TK+/- tumor when administered by 7-day continuous infusion; growth delays of more than 5 days (and some cures) were seen at doses of 25-50 mg/kg/ day. At higher doses, significant wt. loss (gastrointestinal toxicity) and myelosuppression (neutropenia and thrombocytopenia) were obsd., suggesting that these may be dose-limiting toxicities in the Phase I clin. studies.
IT **152946-68-4**, AG337
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(methotrexate transport inhibition and cell growth inhibition by quinazoline thymidylate synthase inhibitors)
RN 152946-68-4 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)



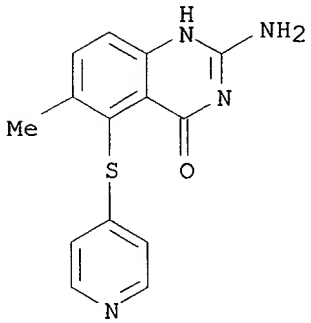
●2 HCl

L14 ANSWER 24 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1996:718933 CAPLUS
DN 126:14419
TI Synergy between the non-classical thymidylate synthase inhibitor AG337 (Thymitaq.RTM.) and cisplatin in human colon and ovarian cancer cells
AU Raymond, Eric; Djelloul, Siham; Buquet-Fagot, Christine; Mester, Jan; Gespach, Christian
CS Inst. Federatif de recherches du Centre Hospitalo, Univ. Paris Saint-Antoine, Paris, 75571, Fr.
SO Anti-Cancer Drugs (1996), 7(7), 752-757
CODEN: ANTDEV; ISSN: 0959-4973
PB Rapid Science Publishers
DT Journal
LA English
AB AG337 is a recent non-classical thymidylate synthase inhibitor with promising activity and manageable toxicity in phase I clin. trials. In this study, we investigated the cytotoxic activity of AG337 alone and in combination with cisplatin in cultured human colon (HT29) and ovarian (2008) cancer cell lines and their derived counterparts selected for this resistance to 5-fluorouracil (5-FU) (HT29-5-FU) and cisplatin (2008C13). We obsd. that AG337 had potent cytotoxic effects in color (IC50 = 0.17 .mu.M) and ovarian cancer cells (IC50 = 0.65 .mu.M). The cytotoxic activity of AG337 was higher than that of 5-FU in the two models. The activity of AG337 was not significantly affected in 5-FU-resistant HT29-5-FU colon cancer cells characterized by an amplification of the thymidylate synthase gene (IC50 = 0.27 .mu.M, p = 0.15). Combinations of cisplatin and AG337 exert synergistic activity in both ovarian and colon cancer cells. Interestingly, this synergism was maintained in 5-FU- and cisplatin-resistant cells. Therefore, our data encourage further examn. of combinations of AG337 with cisplatin in cancer chemotherapy.
IT **152946-68-4**, AG337
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergy between nonclassical thymidylate synthase inhibitor AG337 and cisplatin in human colon and ovarian cancer cells)
RN 152946-68-4 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)



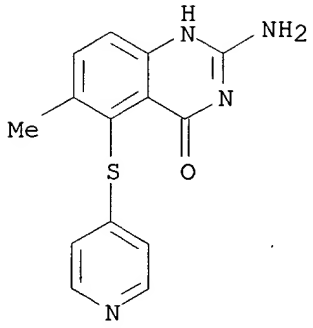
●2 HCl

L14 ANSWER 25 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1996:687846 CAPLUS
DN 125:321447
TI Trichinella spiralis thymidylate synthase: development pattern, isolation, molecular properties, and inhibition by substrate and cofactor analogs
AU Dabrowska, Magdalena; Zielinski, Zbigniew; Wranicz, Mariusz; Michalski, Rafal; Pawelczak, Krzysztof; Rode, Wojciech
CS Nencki Institute Experimental Biology, Polish Academy Sciences, Warsaw, 02-093, Pol.
SO Biochemical and Biophysical Research Communications (1996), 228(2), 440-445
CODEN: BBRCA9; ISSN: 0006-291X
PB Academic
DT Journal
LA English
AB Thymidylate synthase specific activity was found to remain at a const. level in crude exts. from muscle larvae, isolated (1-15 mo after infection) by pepsin-HCl digestion, as well as from adult worms of Trichinella spiralis. The enzyme was purified and its mol. (monomer mol. wt. 35 kDa) and kinetic (sequential mechanism with the Km values 3.1 and 19 .mu.M for dUMP and N5,10-methylenetetrahydrofolate, resp.) properties detd. 5-Fluoro-dUMP was a competitive, slow-binding inhibitor of the parasite enzyme. N5,10-methylenetetrahydrofolate analogs 10-propargyl-5,8-dideazafolate (CB3717), ZD1694, BW1843U89, and AG337 were weaker inhibitors of the parasite than regenerating rat liver enzyme. Inhibition by 10-propargyl-5,8-dideazafolate was strengthened by an increasing no. of glutamate residues. Thymidine kinase activity could not be detected in the muscle larvae crude exts.
IT **152946-68-4**, AG337
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(development pattern, isolation, mol. properties, and inhibition of Trichinella spiralis thymidylate synthase by substrate and cofactor analogs)
RN 152946-68-4 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 26 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1996:611169 CAPLUS
DN 125:296256
TI Modulation of [5-125I]iododeoxyuridine incorporation into tumor and normal tissue DNA by methotrexate and thymidylate synthase inhibitors
AU Mester, J.; DeGoeij, K.; Sluyser, M.
CS INSERM U55, Paris, 75571/12, Fr.
SO European Journal of Cancer, Part A (1996), 32A(9), 1603-1608
CODEN: EJCTEA
PB Elsevier
DT Journal
LA English
AB A potentially useful method for imaging of micrometastases and in situ radiotherapy, would be the incorporation of radioactive labeled iododeoxyuridine (IdU) into tumor DNA. However, there are two main problems: incorporation of the radioactive IdU into normal cells and low incorporation into tumor cells. The aim of this study was to attempt to augment the incorporation of [5-125I]iododeoxyuridine (125IdU) into tumor DNA and to improve the tumor/normal tissue ratio by the use of inhibitors (methotrexate, 5-fluorouracil, AG337, ZD 1694, benzyloxybenzyl uracil) which would prolong the metabolic half-life of the compd. Mammary tumors were induced in GR mice, which were then treated with the inhibitors and the 125IdU. The tumors and representative normal tissue were removed following sacrifice of the animals, and radioactivity within the tissues measured. Pretreatment of mammary carcinoma-bearing GR mice with methotrexate caused approx. a 3-fold increase in the incorporation of 125IdU into tumor DNA, and approx. a .gtoreq.10-fold increase in the tumor/small intestine ratio of incorporated radioactivity. Inhibition of thymidylate synthase, the enzyme involved in IdU dehalogenation, by 5-fluorouracil plus folic acid, or by novel inhibitors AG337 and ZD 1694 led to a 3- to 5-fold increase in the 125IdU incorporation. Benzyloxybenzyl uracil, an inhibitor of dihydrouracil dehydrogenase, had little effect. Treatment of tumor-bearing mice with methotrexate plus ZD 1694 significantly reduced the rate of tumor growth, but addn. of 125IdU (70 .mu.Ci/mouse, three daily injections) had no addnl. antitumor activity. In conclusion, these results do not support the hypothesis that systemic administration of 125IdU can be used for cancer therapy or for imaging purposes unless better methods are found to boost its incorporation into tumor DNA.
IT **152946-68-4**, AG337
RL: BSU (Biological study, unclassified); BIOL (Biological study)
([5-125I]iododeoxyuridine incorporation into mammary carcinoma and normal tissue DNA by methotrexate and thymidylate synthase inhibitors)
RN 152946-68-4 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)

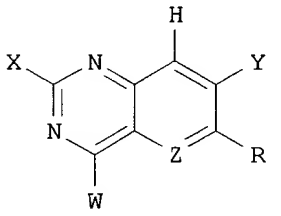


●2 HCl

L14 ANSWER 27 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1996:607480 CAPLUS
DN 125:248328
TI Synthetic triple helix-forming compounds
IN Gold, Barry I.
PA University of Nebraska Board of Regents, USA
SO PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9623777	A1	19960808	WO 1996-US1473	19960129
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE				
	US 5844110	A	19981201	US 1995-384324	19950201
	AU 9647756	A1	19960821	AU 1996-47756	19960129
PRAI	US 1995-384324		19950201		
	WO 1996-US1473		19960129		

OS MARPAT 125:248328
GI



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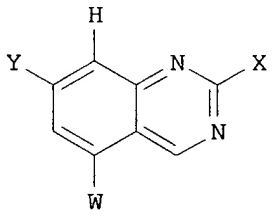
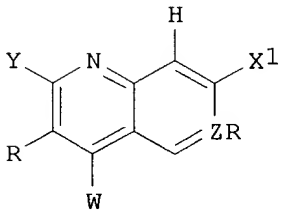
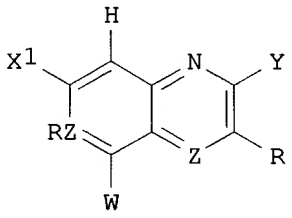


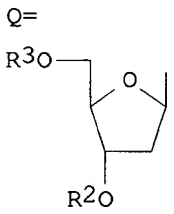
II



III



IV



AB The present invention discloses novel monomeric compns. such as quinazoline derivs. (I and II; X, Y = N, NRR1, OR, SR, PRR1; Z = :CR, :NR; R, R1 = H, CO2H, C6-12 hydrocarbon aryl; W = a substituent that enables linkage of the quinazoline to another quinazoline or quinoline of the invention, preferably via a sugar-phosphate backbone, and is most preferably selected from the group consisting of halo, 2'-deoxy-.beta.-D-ribofuranosyl, 5'-monophospho-2'-deoxy-.beta.-D-ribofuranosyl) and quinoline derivs. (III and IV; X1 = H, CO2-, CS2-; Z =

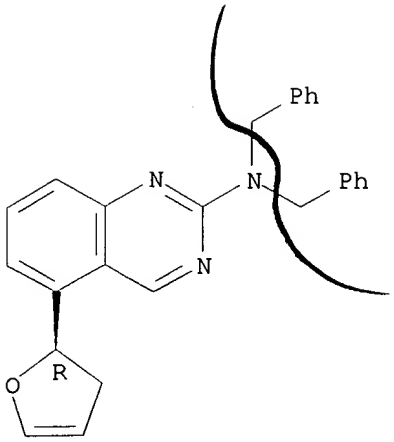
C, N; Y, W = same as above), which are substituted quinoline- or quinazoline-based structures capable of hydrogen bonding specifically with interstrand purine-pyrimidine base pairs in a double-stranded Watson-Crick DNA mol. Preferred monomeric compds. are 2-amino-4-(2'-deoxy-.beta.-D-ribofuranosyl)-7-hydroxyquinazoline (anti-AT), 2-amino-5-(2'-deoxy-.beta.-D-ribofuranosyl)-7-hydroxyquinazoline (anti-TA), 2-amino-4-(2'-deoxy-.beta.-D-ribofuranosyl)-7-carboxyquinoline (anti-GC), and 2-amino-5-(2'-deoxy-.beta.-D-ribofuranosyl)-7-carboxyquinoline (anti-CG), which bind to a target DNA base pair A-T, T-A, G-C, and C-G, resp. Furthermore, the novel monomeric compds. of the present invention are capable of being assembled in specific sequences into oligomers capable of binding with sequence to duplex DNA via a triple helix motif, which may be used for a variety of purposes related to target-specific control of gene expression. Thus, di-Me nitrophthalate and cyanoacetic acid were reacted with NaOMe in MeOH at room temp., followed by Raney nickel redn., chlorination with POCl3 in pyridine under heating, and benzoylation with benzoyl chloride in pyridine to give III (X1 = CO2Me, Y = PhCONH, R = H, Z = C, W = Cl). This compd. in Et2O was treated with BuLi in hexane at room temp. followed by heating for 1 h at reflux temp., and cadmium chloride was added, and the resulting suspension was refluxed for several hours to give, after removing the solvent in vacuo, the organocadmium intermediate. This was treated with 2-deoxy-3,5-di-O-acetyl-.alpha.-D-ribofuranosyl chloride in PhMe and the suspension was refluxed for several h to give III (X1 = CO2Me, Y = PhCONH, R = H, Z = C, W = Q, R2 = R3 = Ac), which was deacetylated with NH3 in MeOH, tritylated by 4,4'-dimethoxytrityl chloride in the presence of 4-dimethylaminopyridine in pyridine, and condensed with 2-cyanoethyl or Me N,N-diisopropylchlorophosphoramidite CH2Cl2 contg. (Me2CH)2NEt to give the anti-GC phosphoramidite III [X1 = CO2Me, Y = PhCONH, R = H, Z = C, W = Q, R2 = P(OCH2CH2CN)N(iso-Pr)2 or P(OMe)N(iso-Pr)2, R3 = 4,4'-dimethoxytrityl]. Using the latter phosphoramidite and other phosphoramidites, oligonucleotide analogs, e.g. poly(anti-TA)12 and 3'-anti(GC-TA-AT-TA-AT-TA-AT-AT-GC-CG-AT-GC), were prepd. by the solid phase method and tested for sequence specific blocking of endonuclease and inhibition of parvovirus transcription.

IT **181871-87-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of amino(deoxyribofuranosyl)hydroxyquinazoline amino(deoxyribofuranosyl)carboxyquinoline and DNA-binding oligonucleotides contg. them as triple helix-forming compds.)

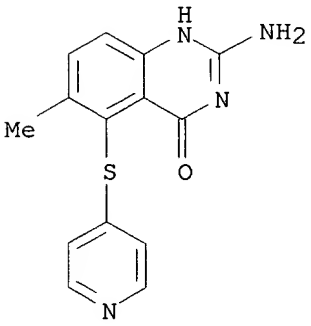
RN 181871-87-4 CAPLUS

CN 2-Quinazolinamine, 5-(2,3-dihydro-2-furanyl)-N,N-bis(phenylmethyl)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.


Ph
N
N
Ph
N
O
R

L14 ANSWER 28 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1996:548480 CAPLUS
DN 125:204236
TI Solid-State Characterization of AG337 (Thymitaq), a Novel Antitumor Drug
AU Dash, Alekha K.; Tyle, Praveen
CS School of Pharmacy and Allied Health Professions, Creighton University, Omaha, NE, 68178, USA
SO Journal of Pharmaceutical Sciences (1996), 85(10), 1123-1127
CODEN: JPMSAE; ISSN: 0022-3549
PB American Chemical Society
DT Journal
LA English
AB AG337 (Thymitaq) was subjected to thermal analyses, Karl Fischer titrimetry, powder x-ray diffractometry, SEM, and FTIR. On the basis of the Karl Fischer and thermogravimetric anal., it was concluded to be a dihydrate. The DSC studies revealed, that on heating, AG337 dehydrates and form a metastable form with a m.p. of 213.degree. followed by crystn. into a stable form at 261.degree.. This stable form was finally melted at 312.degree. with decompn. On the basis of the FTIR and HPLC studies, it was concluded that the final exothermic peak at 320.degree. was due to sample decompn. The powder x-ray diffraction studies confirmed the existence of these 2 polymorphs of AG337. SEM studies revealed that the crystal habits of both the polymorphs were quite different. FTIR spectra of both the polymorphs showed pronounced difference in the range of 600-1800 cm-1.
IT **181360-02-1**
RL: FMU (Formation, unclassified); PRP (Properties); FORM (Formation, nonpreparative)
(solid-state characterization of AG337 as antitumor drug)
RN 181360-02-1 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride, dihydrate (9CI) (CA INDEX NAME)

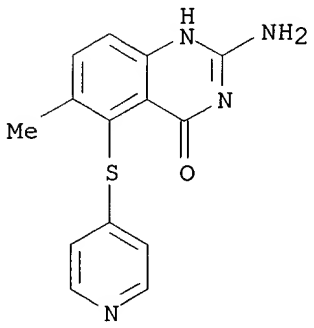


●2 HCl

●2 H_2O

IT **152946-68-4**, AG337
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)
(solid-state characterization of AG337 as antitumor drug)
RN 152946-68-4 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)

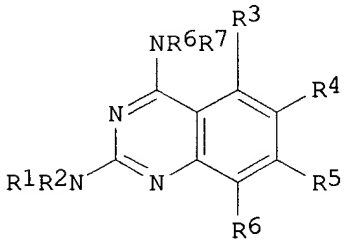


●2 HCl

L14 ANSWER 29 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1996:467270 CAPLUS
DN 125:168006
TI Preparation of 2,4-diaminoquinazolines as insecticides
IN Henrie, Robert N., II; Peake, Clinton J.; Cullen, Thomas G.; Lew, Albert C.; Chaguturu, Munirathnam K.; Ray, Partha S.; Yeager, Walter H.; Silverman, Ian R.; Buser, John W.; et al.
PA FMC Corp., USA
SO U.S., 63 pp., Cont.-in-part of U.S. Ser. No. 149,491, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5534518	A	19960709	US 1994-267340	19940628
	ZA 9401038	A	19940825	ZA 1994-1038	19940215
	US 5616718	A	19970401	US 1995-426541	19950420
	US 5874579	A	19990223	US 1996-640610	19960501
PRAI	US 1993-19389		19930218		
	US 1993-149491		19931109		
	US 1994-267340		19940628		

OS MARPAT 125:168006
GI



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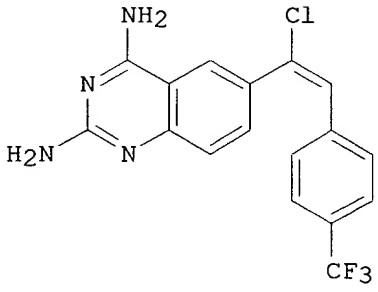


II

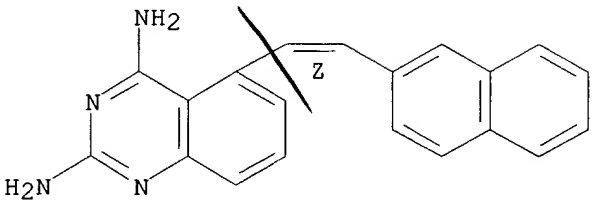
AB Title compds. [I; R1,R6 = H or alkyl; R2,R7 = H, alkyl, alkanoyl, alkoxycarbonyl, etc.; R1R2 = O-interrupted alkylene; R1R2,R6R7 = dialkylaminomethylene, pyrrolidinomethylene, etc.; R3,R5,R6 = H halo, alkyl, alkoxy, etc.; R4 = H halo, alkyl, alkoxy, substituted aryl(oxy), NHCH2C6H4(CO2H)-4, etc.] were prepd. Thus, 2-methyl-6-nitrobenzonitrile was converted in 4 steps to 2-amino-5-ethynyl-6-methylbenzonitrile which was arylated with 4-IC6H4CF3 and the product condensed with ClC(:NH)NH2.HCl to give title compd. II which gave 90 and 100% kill of Trichoplusia ni and Spodoptera exigua, resp., at 30ppm foliar spray.

IT **50828-08-5P 50828-09-6P 50828-12-1P**
50828-13-2P 50828-17-6P 50828-18-7P
50828-19-8P 159018-80-1P 159018-94-7P
159019-13-3P 180269-08-3P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2,4-diaminoquinazolines as insecticides)

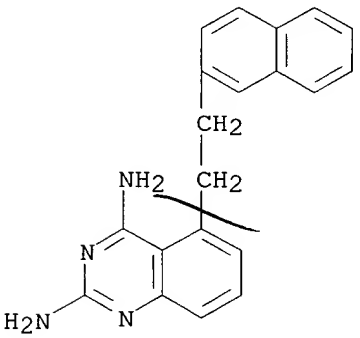
RN 50828-08-5 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethenyl]-, (Z)- (9CI) (CA

INDEX NAME)

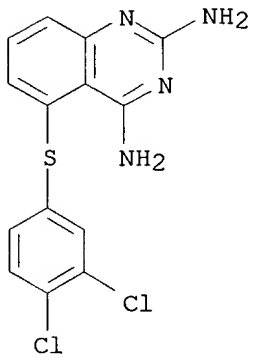
Double bond geometry as shown.



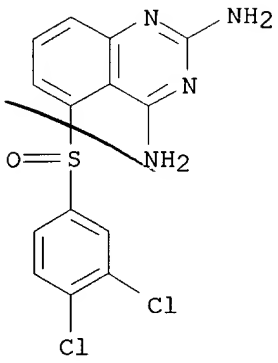
RN 50828-09-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethyl]- (9CI) (CA INDEX NAME)



RN 50828-12-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)thio]- (9CI) (CA INDEX NAME)

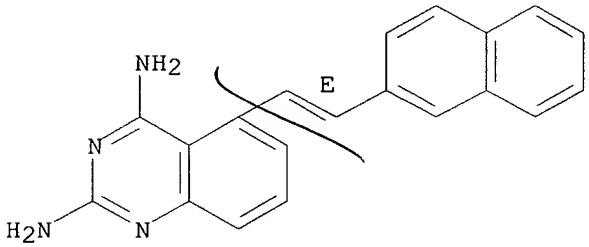


RN 50828-13-2 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)sulfinyl]- (9CI) (CA INDEX NAME)

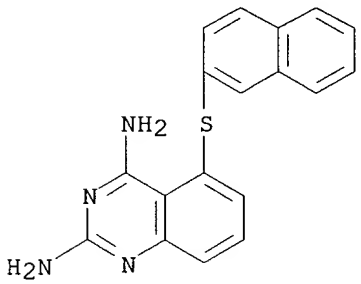


RN 50828-17-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

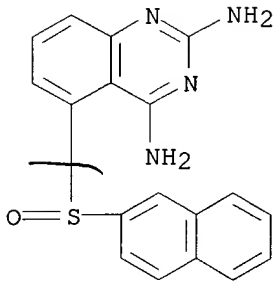
Double bond geometry as shown.



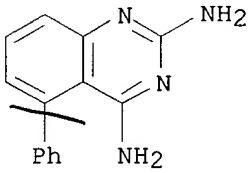
RN 50828-18-7 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)



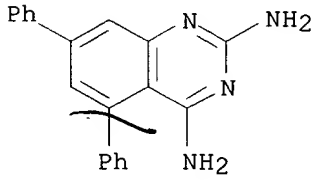
RN 50828-19-8 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylsulfinyl)- (9CI) (CA INDEX NAME)



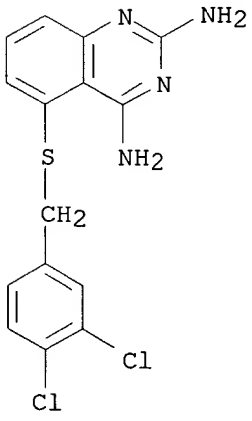
RN 159018-80-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-phenyl- (9CI) (CA INDEX NAME)



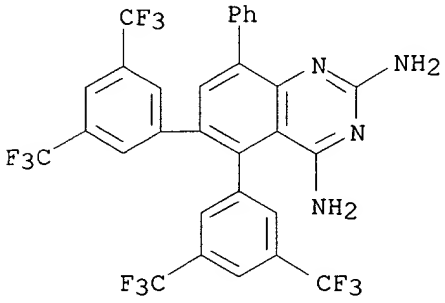
RN 159018-94-7 CAPLUS
CN 2,4-Quinazolinediamine, 5,7-diphenyl- (9CI) (CA INDEX NAME)



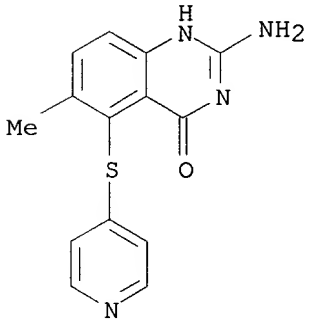
RN 159019-13-3 CAPLUS
CN 2,4-Quinazolinediamine, 5-[[(3,4-dichlorophenyl)methyl]thio]- (9CI) (CA INDEX NAME)



RN 180269-08-3 CAPLUS
CN 2,4-Quinazolinediamine, 5,6-bis[3,5-bis(trifluoromethyl)phenyl]-8-phenyl- (9CI) (CA INDEX NAME)

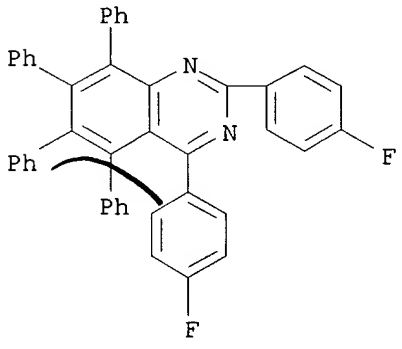


L14 ANSWER 30 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1996:402803 CAPLUS
DN 125:67497
TI A cubic-phase oral drug delivery system for controlled release of AG337
AU Longer, Mark; Tyle, Praveen; Mauger, John W.
CS Pharmaceutical Development Dep., Agouron Pharmaceuticals Inc., La Jolla, CA, 92037, USA
SO Drug Development and Industrial Pharmacy (1996), 22(7), 603-608
CODEN: DDIPD8; ISSN: 0363-9045
PB Dekker
DT Journal
LA English
AB AG337 is a novel thymidylate synthase inhibitor with antitumor activity which was designed by using protein structure-based techniques. It is currently undergoing clin. trials as both i.v. and oral formulations. Based on the short in vivo half-life of AG337, an oral controlled-release formulation is desired. The feasibility of using cubic liq. cryst. phases formed from monoolein for controlled release of AG337 was investigated in this study. AG337 (m.p. 298.degree.) was triturated with glycerol and then dissolved in monoolein using mild heat. The resulting gel was liquefied by further heating to 65.degree., then cooled to RT to yield a clear viscous soln. Samples of the formulation were exposed to water for up to 48 h at 25.degree.. Thermal anal. of this system was undertaken in order to det. the effect of hydration state on the liq. cryst. structure. The DSC profile of samples not exposed to water showed no distinct endo- or exothermic transitions. However, samples exposed to water exhibited multiple endothermic transitions from 80 to 120.degree.. These data demonstrate a thermal response to time-dependent water uptake in the formulation as might occur in vivo after oral dosing, due to changes in phys. properties of the system. In vitro release rates of AG337 from this formulation were evaluated.
IT **152946-68-4**, AG337
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cubic-phase oral drug delivery system for controlled release of AG337)
RN 152946-68-4 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 31 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1996:390278 CAPLUS
DN 125:143468
TI Thermal chemistry of poly(aryl ether phthalazine)s and the synthesis of poly(aryl ether quinazoline)s
AU Chan, Kwok P.; Yang, Haixin; Hay, Allan S.
CS Dep. Chem., McGill Univ., Montreal, QC, H3A 2K6, Can.
SO Journal of Polymer Science, Part A: Polymer Chemistry (1996), 34(10), 1923-1931
CODEN: JPACEC; ISSN: 0887-624X
PB Wiley
DT Journal
LA English
AB Poly(aryl ether phthalazines) underwent an exothermic reaction at 360-440.degree.. The origin of the exothermic reaction and the physiochem. phenomena assocd. with it were elucidated based on thermal analyses, model compd. studies, and 13C solid-state NMR studies. At elevated temps., polymers contg. a diphenylphthalazine moiety underwent extensive thermal crosslinking reactions as a result of a nitrogen elimination reaction of the phthalazine moiety. However, polymers contg. tetra-Ph or hexaphenyl phthalazine moieties underwent principally a backbone rearrangement reaction, in which the phthalazine moiety rearranged to a quinazoline. Utilizing this efficient thermal rearrangement of polyphenylated phthalazines, a novel activated difluoride, 2,4-bis(4-fluorophenyl)-5,6,7,8-tetraphenylquinazoline, which underwent high-temp. soln. polycondensation with bisphenol A to give the quinazoline-contg. poly(aryl ether) (I). I is amorphous, has Tg 265.degree., and has high thermooxidative stability with 5% wt. loss being recorded at 514.degree. in nitrogen.
IT **163930-43-6P**
RL: NUU (Other use, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(monomer and model compd.; thermal rearrangement of phenylphthalazines as model for poly(aryl ether phthalazines))
RN 163930-43-6 CAPLUS
CN Quinazoline, 2,4-bis(4-fluorophenyl)-5,6,7,8-tetraphenyl- (9CI) (CA INDEX NAME)

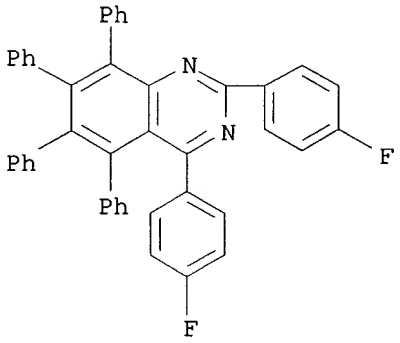


IT **179796-17-9P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and characterization of poly(aryl ether phthalazines) in relation to thermal crosslinking and rearrangements)

RN 179796-17-9 CAPLUS
CN Phenol, 4,4'-(1-methylethylidene)bis-, polymer with 2,4-bis(4-fluorophenyl)-5,6,7,8-tetraphenylquinazoline (9CI) (CA INDEX NAME)

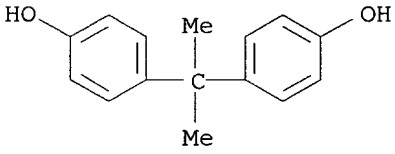
CM 1

CRN 163930-43-6
CMF C44 H28 F2 N2

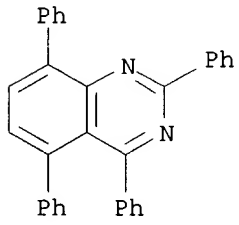


CM 2

CRN 80-05-7
CMF C15 H16 O2

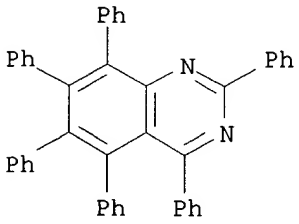


IT **163930-41-4P**, 2,4,5,8-Tetraphenylquinazoline **163930-42-5P**
RL: NUU (Other use, unclassified); SPN (Synthetic preparation); PREP (Preparation); USES (Uses)
(thermal rearrangement of phenylphthalazines as model for poly(aryl ether phthalazines))
RN 163930-41-4 CAPLUS
CN Quinazoline, 2,4,5,8-tetraphenyl- (9CI) (CA INDEX NAME)



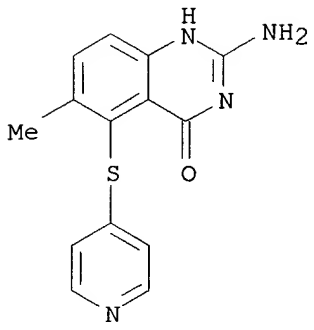
RN 163930-42-5 CAPLUS

CN Quinazoline, hexaphenyl- (9CI) (CA INDEX NAME)



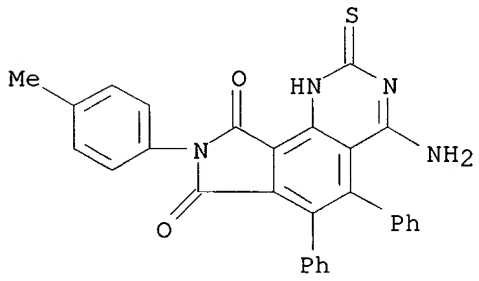
L14 ANSWER 32 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1996:244985 CAPLUS
DN 124:332076
TI AG337, a novel lipophilic thymidylate synthase inhibitor: In vitro and in vivo preclinical studies
AU Webber, Stephanie; Bartlett, Charlotte A.; Boritzki, Theodore J.; Hilliard, Jill A.; Howland, Eleanor F.; Johnston, Amanda L.; Kosa, Maha; Margosiak, Stephen A.; Morse, Cathy A.; Shetty, Bhasker V.
CS Pharmacology Department, Agouron Pharmaceuticals, Inc., San Diego, CA, 92121, USA
SO Cancer Chemother. Pharmacol. (1996), 37(6), 509-17
CODEN: CCPHDZ; ISSN: 0344-5704
DT Journal
LA English
AB 3,4-Dihydro-2-amino-6-methyl-4-oxo-5-(4-pyridylthio)-quinazoline dihydrochloride (AG337) is a water-sol., lipophilic inhibitor of thymidylate synthase (TS) designed using X-ray structure-based methodologies to interact at the folate cofactor binding site of the enzyme. The aim of the design program was to identify TS inhibitors with different pharmacol. characteristics from classical folate analogs and, most notably, to develop non-glutamate-contg. mols. which would not require facilitated transport for uptake and would not undergo intracellular polyglutamylation. One mol. which resulted from this program, AG337, inhibits purified recombinant human TS with a Ki of 11 nM, and displays non-competitive inhibition kinetics. It was further shown to inhibit cell growth in a panel of cell lines of murine and human origin, displaying an IC50 of between 0.39 .mu.M and 6.6 .mu.M. TS was suggested as the locus of action of AG337 by the ability of thymidine to antagonize cell growth inhibition and the direct demonstration of TS inhibition in whole cells using a tritium release assay. The demonstration, by flow cytometry, that AG337-treated L1210 cells were arrested in the S phase of the cell cycle was also consistent with a blockage of TS, as was the pattern of ribonucleotide and deoxyribonucleotide pool modulation in AG337-treated cells, which showed significant redn. in TTP levels. The effects of AG337 were quickly reversed on removal of the drug, suggesting, as would be expected for a lipophilic agent, that there is rapid influx and efflux from cells and no intracellular metab. to derivs. with enhanced retention. In vivo, AG337 was highly active against the thymidine kinase-deficient murine L5178Y/TK- lymphoma implanted either i.p. or i.m. following i.p. or oral delivery. Prolonged dosing periods of 5 or 10 days were required for activity, and efficacy was improved with twice-daily dose administration. Dose levels of 25 mg/kg delivered i.p. twice daily for 10 days, 50 mg/kg once daily for 10 days, or 100 mg/kg once daily for 5 days elicited 100% cures against the i.p. tumor. Doses required for activity against the i.m. tumor were higher (100 mg/kg i.p. twice daily for 5 or 10 days) but demonstrated the ability of AG337 to penetrate solid tissue barriers. Oral delivery required doses of .gtoreq. 150 mg/kg twice daily for periods of 5-10 days to produce 100% cure rates against both i.m. and i.p. implanted tumors. These results were consistent with the pharmacokinetic parameters detd. in rats, for which oral bioavailability of 30-50% was detd., together with a relatively short elimination half life of 2 h. Clin. studies with AG337 are currently in progress.
IT **152946-68-4**, AG337
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antitumor activity of thymidylate synthase inhibitor AG337)
RN 152946-68-4 CAPLUS

CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)

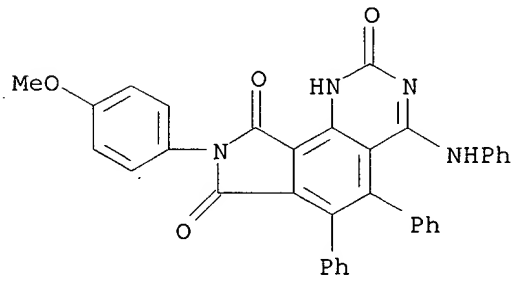


●2 HCl

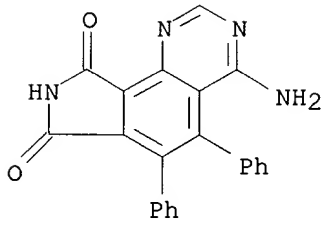
L4 ANSWER 33 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1996:149542 CAPLUS
DN 124:289477
TI Synthesis of New Fused Isoindolinedione Derivatives
AU Ali, M. M.; Zahran, M. A.; Afifi, T. H.; Seliem, A. H. T.
CS Faculty Science, Al-Azhar University, Nasr City, Egypt
SO Al-Azhar J. Pharm. Sci. (1994), 14, 100-7
CODEN: AAJPFT; ISSN: 1110-1644
DT Journal
LA English
AB Condensation of 6-amino-5-cyano-3,4-diphenyl phthalic anhydride [i.e., 5-amino-1,3-dihydro-1,3-dioxo-6,7-diphenyl-5-isobenzofurancarbonitrile] with amines in acetic acid resulted in the formation of N-arylisoindolinediones. Cyclization with urea and thiourea gave N-arylisoindolinopyrimidine derivs. A reaction N-arylisoindolinediones with formamide, urea and thiourea furnished isoindolinopyrimidine derivs.
IT **175851-10-2P 175851-11-3P 175851-12-4P**
175851-13-5P 175851-14-6P 175851-17-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of fused isoindolinedione derivs.)
RN 175851-10-2 CAPLUS
CN 1H-Pyrrolo[3,4-h]quinazoline-7,9(2H,8H)-dione, 4-amino-8-(4-methylphenyl)-5,6-diphenyl-2-thioxo- (9CI) (CA INDEX NAME)



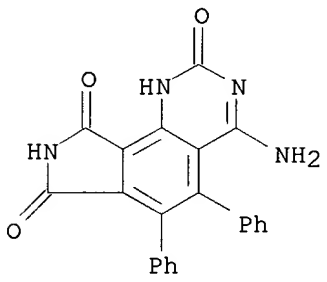
RN 175851-11-3 CAPLUS
CN 1H-Pyrrolo[3,4-h]quinazoline-2,7,9(8H)-trione, 8-(4-methoxyphenyl)-5,6-diphenyl-4-(phenylamino)- (9CI) (CA INDEX NAME)



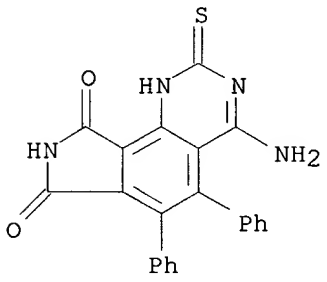
RN 175851-12-4 CAPLUS
CN 7H-Pyrrolo[3,4-h]quinazoline-7,9(8H)-dione, 4-amino-5,6-diphenyl- (9CI) (CA INDEX NAME)



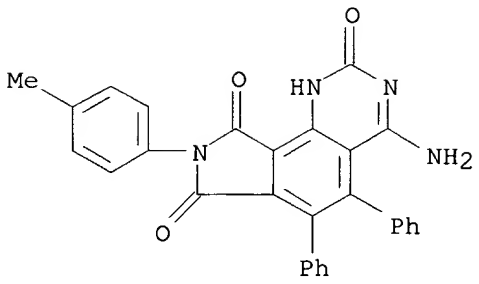
RN 175851-13-5 CAPLUS
CN 1H-Pyrrolo[3,4-h]quinazoline-2,7,9(8H)-trione, 4-amino-5,6-diphenyl- (9CI) (CA INDEX NAME)



RN 175851-14-6 CAPLUS
CN 1H-Pyrrolo[3,4-h]quinazoline-7,9(2H,8H)-dione, 4-amino-5,6-diphenyl-2-thioxo- (9CI) (CA INDEX NAME)



RN 175851-17-9 CAPLUS
CN 1H-Pyrrolo[3,4-h]quinazoline-2,7,9(8H)-trione, 4-amino-8-(4-methylphenyl)-5,6-diphenyl- (9CI) (CA INDEX NAME)


Me
O
HN
N
NH2
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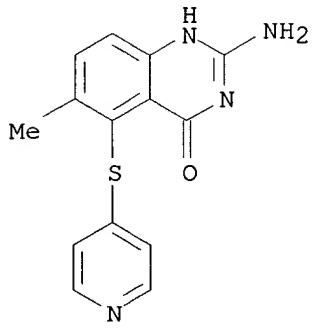
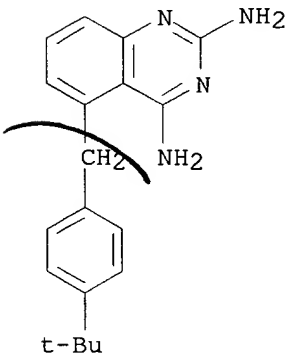
Ph
Ph
O

L14> ANSWER 34 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1996:39928 CAPLUS
DN 124:164193
TI Clinical pharmacokinetic and pharmacodynamic studies with the nonclassical antifolate thymidylate synthase inhibitor 3,4-dihydro-2-amino-6-methyl-4-oxo-5-(4-pyridylthio)-quinazolone dihydrochloride (AG337) given by 24-hour continuous intravenous infusion
AU Rafi, Imran; Taylor, Gordon A.; Calvete, Joanne A.; Boddy, Alan V.; Balmanno, Kathryn; Bailey, Nigel; Lind, Michael; Calvert, A. Hilary; Webber, Stephanie; et al.
CS Medical School, University Newcastle upon Tyne, Newcastle, NE2 4HH, UK
SO Clin. Cancer Res. (1995), 1(11), 1275-84
CODEN: CCREF4; ISSN: 1078-0432
DT Journal
LA English
AB 3,4-Dihydro-2-amino-6-methyl-4-oxo-5-(4-pyridylthio)-quinazolone dihydrochloride (AG337) is a nonclassical inhibitor of thymidylate synthase (TS) designed to avoid potential resistance mechanisms that can limit the activity of classical antifolate antimetabolites. A clin. pharmacokinetic and pharmacodynamic study of AG337 given as a 24-h i.v. infusion was performed. Thirteen patients received 27 courses over the dose range 75-1350 mg/m2. Plasma AG337 concns. were achieved which, in preclin. models, were assocd. with antitumor effects. AG337 clearance was saturable, and the pharmacokinetics of the drug at doses above 300 mg/m2 was best described by a one-compartment model with saturable elimination (median Km = 6.5 .mu.g/mL; range, 4.1-13 .mu.g/mL; median Vmax = 2.0 .mu.g/mL/ h/m2; range, 0.96-5.6 .mu.g/mL/h/m2). Following the end of the infusion, AG337 was cleared rapidly (t1/2, 53-193 min), and levels were less than 0.2 .mu.g/mL in all patients by 48 h. Plasma protein binding was 96-98%, and the urinary excretion of AG337 as unchanged drug did not exceed 30% of the dose administered. Measurements of plasma deoxyuridine (dUrd) concns. showed that doses of 600 mg/m2 and above of AG337 produced a consistent elevation in plasma dUrd levels (60-290%), suggesting that TS inhibition was being achieved in patients. However, in all cases dUrd concns. had returned to pretreatment levels 24 h after the end of the infusion, suggesting that TS inhibitions was not maintained. Local toxicity, probably due to the infusate pH, was the only significant adverse effect obsd. These studies have shown that cytotoxic AG337 plasma concns. can be readily achieved without acute toxicity and that these concns. are assocd. with elevations in plasma dUrd levels. The lack of prolonged dUrd elevations indicates that extended administration should be explored using central line or p.o. administration to avoid local toxicity.
IT **152946-68-4**, AG337
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clin. pharmacokinetic and pharmacodynamic studies with nonclassical antifolate thymidylate synthase inhibitor 3,4-dihydro-2-amino-6-methyl-4-oxo-5-(4-pyridylthio)-quinazolone dihydrochloride (AG337) given by continuous infusion in humans)
RN 152946-68-4 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)

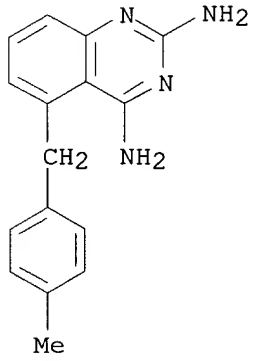


●2 HCl

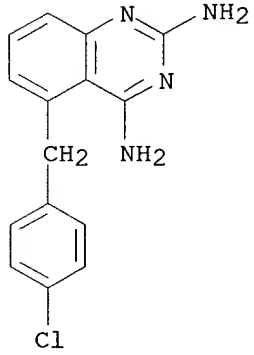
L14 ANSWER 35 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1995:945313 CAPLUS
DN 124:146047
TI Synthesis of 5-(4-substituted benzyl)-2,4-diaminoquinazolines as inhibitors of Candida albicans dihydrofolate reductase
AU Jagdmann, G. Erik, Jr.; Chan, Joseph H.; Styles, Virgil L.; Tansik, Robert L.; Boytos, Christine M.; Rudolph, Sharon K.
CS Divisions of Organic Chemistry, Burroughs Wellcome Co., Research Triangle Park, NC, 27709, USA
SO J. Heterocycl. Chem. (1995), 32(5), 1461-5
CODEN: JHTCAD; ISSN: 0022-152X
DT Journal
LA English
OS CASREACT 124:146047
AB Several 5-(4-substituted benzyl)-2,4-diaminoquinazolines (6) were prepd. as potentially selective inhibitors of Candida albicans dihydrofolate reductase. These compds. were synthesized by a novel route, which included as a key step the displacement of a fluoro group in 2,6-difluorobenzonitrile by the anions of Et or Me 4-substituted phenylacetates. The resultant diarylacetates were sapond. and decarboxylated to the 2-fluoro-6-(4-substituted phenyl)benzonitriles. Ring closure of these benzonitriles with guanidine carbonate gave 6.
IT **173206-06-9P 173206-07-0P 173206-08-1P**
173206-09-2P 173206-10-5P 173206-11-6P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of (substituted benzyl)diaminoquinazolines as inhibitors of Candida albicans dihydrofolate reductase)
RN 173206-06-9 CAPLUS
CN 2,4-Quinazolinediamine, 5-[[4-(1,1-dimethylethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



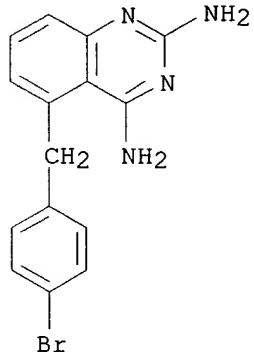
RN 173206-07-0 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(4-methylphenyl)methyl]- (9CI) (CA INDEX NAME)



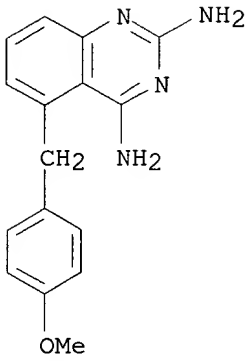
RN 173206-08-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(4-chlorophenyl)methyl]- (9CI) (CA INDEX NAME)



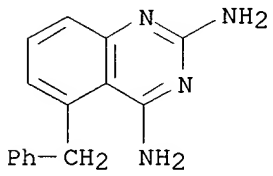
RN 173206-09-2 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(4-bromophenyl)methyl]- (9CI) (CA INDEX NAME)



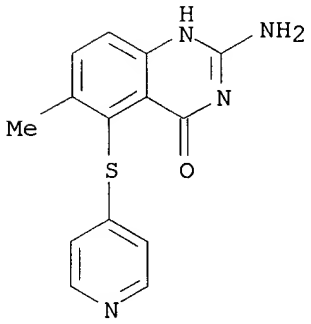
RN 173206-10-5 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



RN 173206-11-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-(phenylmethyl)- (9CI) (CA INDEX NAME)



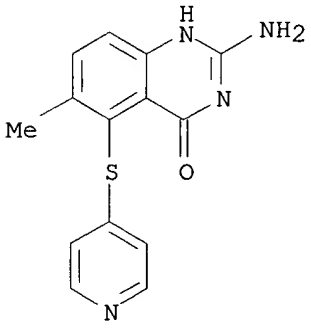
L14 ANSWER 36 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1995:936400 CAPLUS
DN 124:21268
TI Cross-resistance to thymidylate synthase inhibitors in P-glycoprotein and non-P-glycoprotein cell lines
AU Van Triest, B.; Telleman, F.; Pinedo, H. M.; Van der Wilt, C. L.; Peters, G. J.
CS Department Medical Oncology, Free University Hospital, Amsterdam, 1007 MB, Neth.
SO Advances in Experimental Medicine and Biology (1994), 370(Purine and Pyrimidine Metabolism in Man VIII), 189-93
CODEN: AEMBAP; ISSN: 0065-2598
PB Plenum
DT Journal
LA English
AB We selected a panel of 3 cell lines, the wild type SW1573 and 2 doxorubicin (DOX) resistant cell lines; a MDR variant resistant to DOX due to P-gp overexpression (SW1573/2R160) and a subline resistant to DOX but with no P-gp overexpression (SW1573/2R120). In these cell lines we detd. whether they exhibit a cross-resistance to 5-fluorouracil. We also detd. a possible cross-resistance to several TS-inhibitors with different structural properties; ZD1694 (Tomudex) an antifolate dependent on transport via the reduced folate carrier and a good substrate for folylpolyglutamate synthetase; and AG337 a lipophilic compd., transported by passive diffusion which cannot be polyglutamylated.
IT **152946-68-4**, AG337
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(cross-resistance to thymidylate synthase inhibitors in P-glycoprotein and non-P-glycoprotein cell lines)
RN 152946-68-4 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

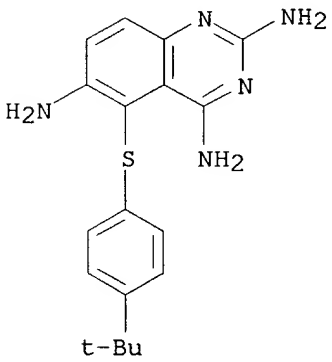
L14 ANSWER 37 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1995:846299 CAPLUS
DN 123:329253
TI Carrier- and receptor-mediated transport of folate antagonists targeting folate-dependent enzymes: correlates of molecular-structure and biological activity
AU Westerhof, G. Robbin; Schornagel, Jan H.; Kathmann, Ietje; Jackman, Ann L.; Rosowsky, Andre; Forsch, Ronald A.; Hynes, John B.; Boyle, F. Thomas; Peters, Godefridus J.; et al.
CS Department Oncology, University Hospital Vrije Universiteit, Amsterdam, 1007 MB, Neth. Sept.
SO Mol. Pharmacol. (1995), 48(3), 459-71
CODEN: MOPMA3; ISSN: 0026-895X
DT Journal
LA English
AB The transport properties and growth-inhibitory potential of 37 classic and novel antifolate compds. have been tested in vitro against human and murine cell lines expressing different levels of the reduced folate carrier (RFC), the membrane-assocd. folate binding protein (mFBP), or both. The intracellular targets of these drugs were dihydrofolate reductase (DHFR), glycinamide ribonucleotide transformylase (GARTF), folylpolyglutamate synthetase (FPGS), and thymidylate synthase (TS). Parameters that were investigated included the affinity of both folate-transport systems for the antifolate drugs, their growth-inhibitory potential as a function of cellular RFC/mFBP expression, and the protective effect of either FA or leucovorin against growth inhibition. Methotrexate, aminopterin, N10-propargyl-5,8-dideazafolic acid (CB3717), ZD1694, 5,8-dideazaisofolic acid (IAHQ), 5,10-dideazatetrahydrofolic acid (DDATHF), and 5-deazafolic acid (efficient substrate for FPGS) were used as the basic structures in the present study, from which modifications were introduced in the pteridine/quinazoline ring, the C9-N10 bridge, the benzoyl ring, and the glutamate side chain. It was obsd. that RFC exhibited an efficient substrate affinity for all analogs except CB3717, 2-NH2ZD1694, and glutamate side-chain-modified FPGS inhibitors. Substitutions at the 2-position (e.g., 2-CH3) improved the RFC substrate affinity for methotrexate and aminopterin. Other good substrates included PT523 (N.alpha.-(4-amino-4-deoxypteroyl)-N.delta.-hemiphthaloyl-L-ornithine), 10-ethyl-10-deazaaminopterin, and DDATHF. With respect to mFBP, modifications at the N-3 and 4-oxo positions resulted in a substantial loss of binding affinity. Modifications at other sites of the mol. were well tolerated. Growth-inhibition studies identified a series of drugs that were preferentially transported via RFC (2,4-diamino structures) or mFBP (CB3717, 2-NH2-ZD1694, or 5,8-dideazaisofolic acid), whereas other drugs were efficiently transported via both transport pathways (e.g., DDATHF, ZD1694, BW1843U89, or LY231514). Given the fact that for an increasing no. of normal and neoplastic cells and tissues, different expression levels of RFC and mFBP are being recognized, this folate antagonist structure-activity relation can be value for predicting drug sensitivity and resistance of tumor cells or drug-related toxicity to normal cells and for the rational design and development of novel antifolates.
IT **152946-68-4**, AG 337
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(structure activity relations of carrier- and receptor-mediated transport of antifolate drugs and antitumor activity)
RN 152946-68-4 CAPLUS

CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 38 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1995:746895 CAPLUS
DN 123:256633
TI Selective Inhibitors of Candida albicans Dihydrofolate Reductase: Activity and Selectivity of 5-(Arylthio)-2,4-diaminoquinazolines
AU Chan, Joseph H.; Hong, Jean S.; Kuyper, Lee F.; Baccanari, David P.; Joyner, Suzanne S.; Tansik, Robert L.; Boytos, Christine M.; Rudolph, Sharon K.
CS Division of Organic Chemistry, Burroughs Wellcome Company, Research Triangle Park, NC, 27709, USA
SO J. Med. Chem. (1995), 38(18), 3608-16
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
AB The recent increase in fungal infections, esp. among AIDS patients, has resulted in the need for more effective antifungal agents. This search for such agents was focused on developing compds. which inhibit fungal dihydrofolate reductase (DHFR). A series of 25 5-(arylthio)-2,4-diaminoquinazolines were synthesized as potentially selective inhibitors of Candida albicans DHFR. The majority of the compds. were potent inhibitors of C. albicans DHFR and much less active against human DHFR. High selectivity, as defined by the ratio of the I50 values for human and C. albicans DHFR, was achieved by compds. with bulky and rigid 4-substituents in the phenylthio moiety. For example, 5-[(4-morpholinophenyl)thio]-2,4-diaminoquinazoline displayed a selectivity ratio of 540 and was the most selective inhibitor synthesized to date. Substitution in the 2- or 3-position of the 5-phenylthio group provided only marginal selectivity. 6-Substituted-5-[(4-tert-butylphenyl)thio]-2,4-diaminoquinazolines showed potent activity against the C. albicans enzyme but were equally active against human DHFR. Most of the selective compds. were also good inhibitors of C. albicans cell growth, with min. inhibitory concn. values as low as 0.05 .mu.g/mL.
IT **168910-93-8P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(5-[(4-(1,1-dimethylethyl)phenyl]thio]-2,4,6-quinazolinetriamine; prepn. of (arylthio)quinazolinediamines as fungicides)
RN 168910-93-8 CAPLUS
CN 2,4,6-Quinazolinetriamine, 5-[[4-(1,1-dimethylethyl)phenyl]thio]- (9CI) (CA INDEX NAME)

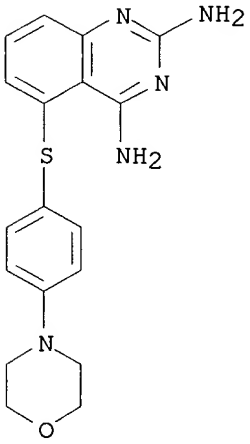


IT **168910-28-9P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(5-[(4-morpholinophenyl)thio]-2,4-quinazolinediamine; prepn. of (arylthio)quinazolinediamines as fungicides)

RN 168910-28-9 CAPLUS

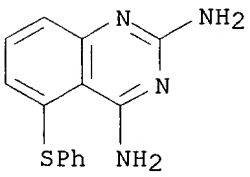
CN 2,4-Quinazolinediamine, 5-[[4-(4-morpholinyl)phenyl]thio]- (9CI) (CA INDEX NAME)



IT **123241-99-6P**, 2,4-Quinazolinediamine, 5-(phenylthio)
168910-32-5P 168910-33-6P 168910-34-7P
168910-35-8P 168910-36-9P 168910-37-0P
168910-38-1P 168910-39-2P 168910-48-3P
168910-49-4P 168910-50-7P 168910-51-8P
168910-52-9P 168910-53-0P 168910-54-1P
168910-55-2P 168910-56-3P 168910-57-4P
168910-58-5P 168910-59-6P 168910-60-9P
168910-61-0P 168910-62-1P 168910-94-9P
168910-95-0P 168910-96-1P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of (arylthio)quinazolinediamines as fungicides)

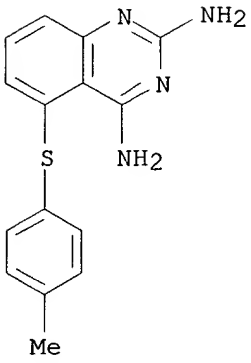
RN 123241-99-6 CAPLUS

CN 2,4-Quinazolinediamine, 5-(phenylthio)- (9CI) (CA INDEX NAME)

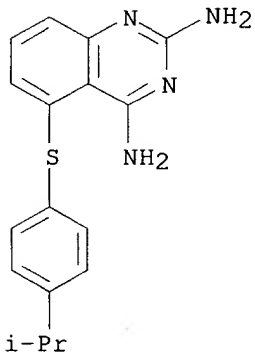


RN 168910-32-5 CAPLUS

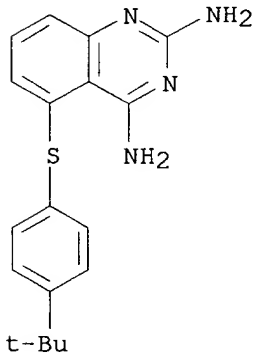
CN 2,4-Quinazolinediamine, 5-[(4-methylphenyl)thio]- (9CI) (CA INDEX NAME)



RN 168910-33-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-[[4-(1-methylethyl)phenyl]thio]- (9CI) (CA INDEX NAME)

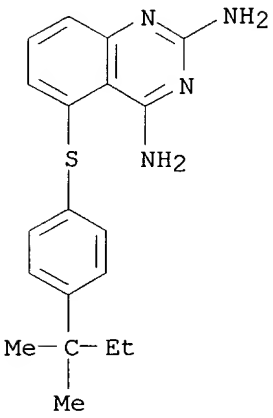


RN 168910-34-7 CAPLUS
CN 2,4-Quinazolinediamine, 5-[[4-(1,1-dimethylethyl)phenyl]thio]- (9CI) (CA INDEX NAME)

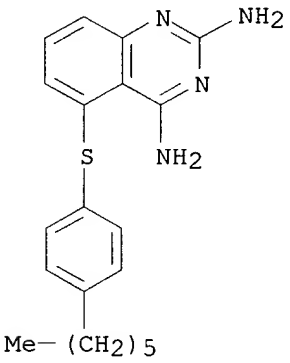


RN 168910-35-8 CAPLUS
CN 2,4-Quinazolinediamine, 5-[[4-(1,1-dimethylpropyl)phenyl]thio]- (9CI) (CA

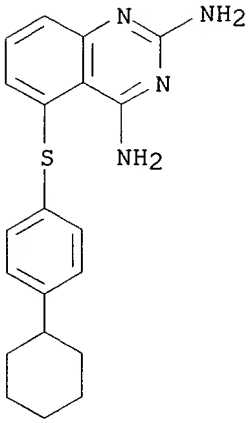
INDEX NAME)



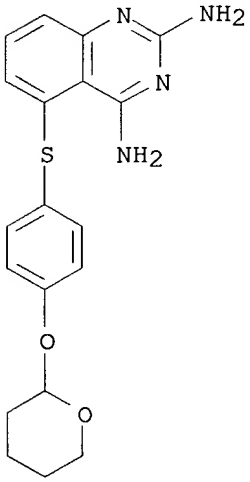
RN 168910-36-9 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(4-hexylphenyl)thio]- (9CI) (CA INDEX NAME)



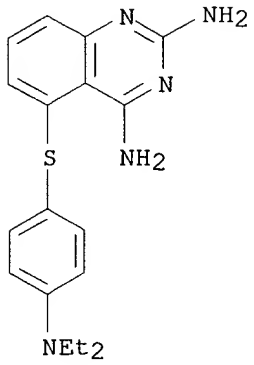
RN 168910-37-0 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(4-cyclohexylphenyl)thio]- (9CI) (CA INDEX NAME)



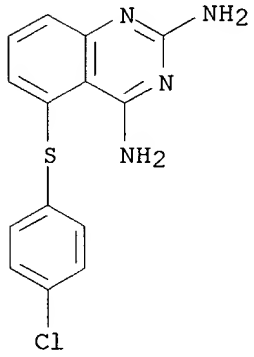
RN 168910-38-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-[[4-[(tetrahydro-2H-pyran-2-yl)oxy]phenyl]thio]- (9CI) (CA INDEX NAME)



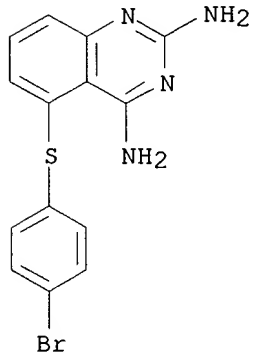
RN 168910-39-2 CAPLUS
CN 2,4-Quinazolinediamine, 5-[[4-(diethylamino)phenyl]thio]- (9CI) (CA INDEX NAME)



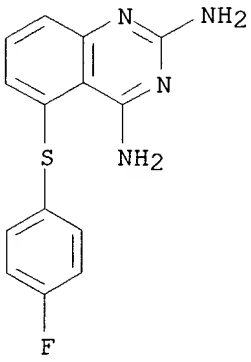
RN 168910-48-3 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(4-chlorophenyl)thio]- (9CI) (CA INDEX NAME)



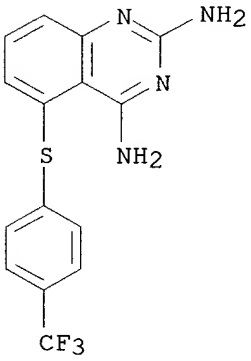
RN 168910-49-4 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(4-bromophenyl)thio]- (9CI) (CA INDEX NAME)



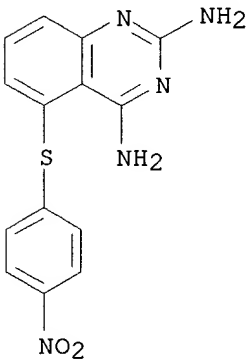
RN 168910-50-7 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(4-fluorophenyl)thio]- (9CI) (CA INDEX NAME)



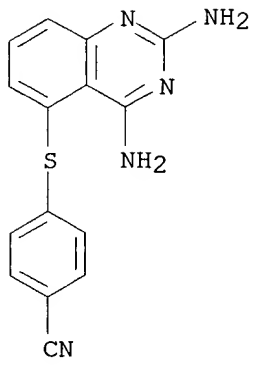
RN 168910-51-8 CAPLUS
CN 2,4-Quinazolinediamine, 5-[[4-(trifluoromethyl)phenyl]thio]- (9CI) (CA INDEX NAME)



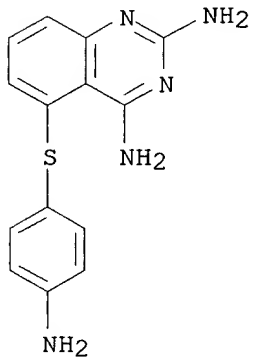
RN 168910-52-9 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(4-nitrophenyl)thio]- (9CI) (CA INDEX NAME)



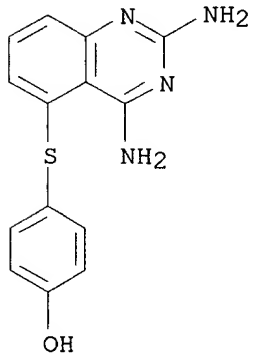
RN 168910-53-0 CAPLUS
CN Benzonitrile, 4-[(2,4-diamino-5-quinazolinyl)thio]- (9CI) (CA INDEX NAME)



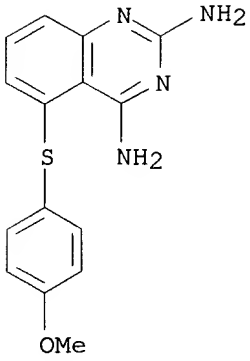
RN 168910-54-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(4-aminophenyl)thio]- (9CI) (CA INDEX NAME)



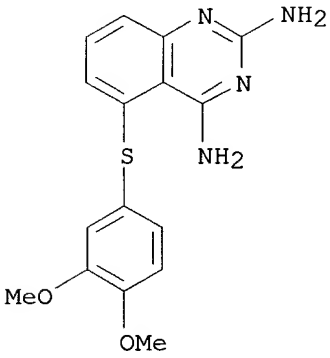
RN 168910-55-2 CAPLUS
CN Phenol, 4-[(2,4-diamino-5-quinazolinyl)thio]- (9CI) (CA INDEX NAME)



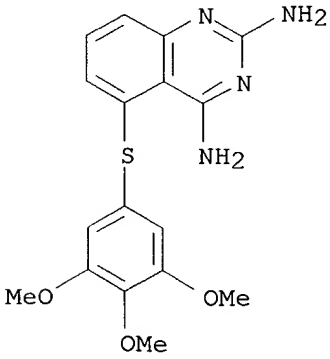
RN 168910-56-3 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(4-methoxyphenyl)thio]- (9CI) (CA INDEX NAME)



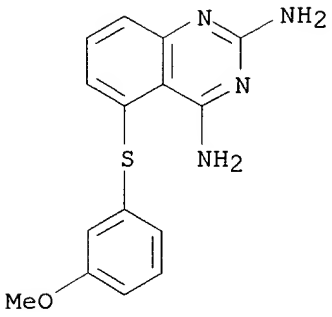
RN 168910-57-4 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dimethoxyphenyl)thio]- (9CI) (CA INDEX NAME)



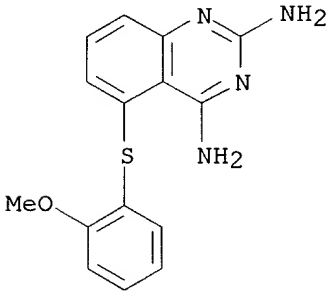
RN 168910-58-5 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4,5-trimethoxyphenyl)thio]- (9CI) (CA INDEX NAME)



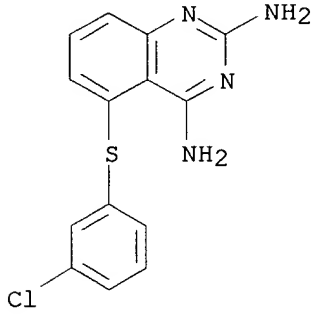
RN 168910-59-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3-methoxyphenyl)thio]- (9CI) (CA INDEX NAME)



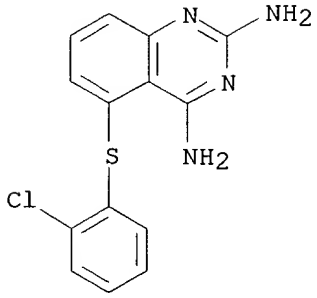
RN 168910-60-9 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(2-methoxyphenyl)thio]- (9CI) (CA INDEX NAME)



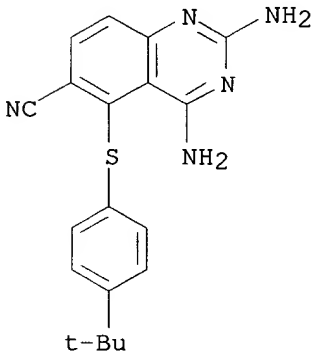
RN 168910-61-0 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3-chlorophenyl)thio]- (9CI) (CA INDEX NAME)



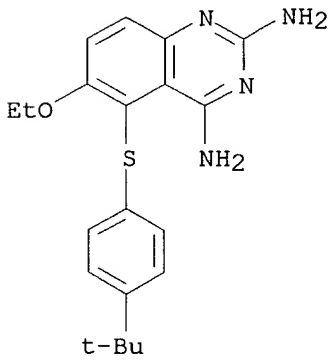
RN 168910-62-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(2-chlorophenyl)thio]- (9CI) (CA INDEX NAME)



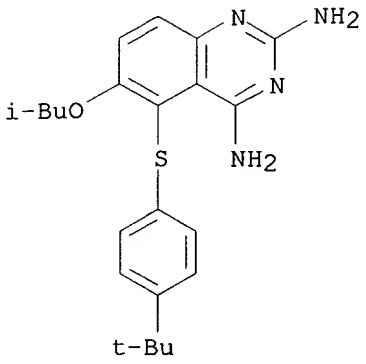
RN 168910-94-9 CAPLUS
CN 6-Quinazolinecarbonitrile, 2,4-diamino-5-[[4-(1,1-dimethylethyl)phenyl]thio]- (9CI) (CA INDEX NAME)



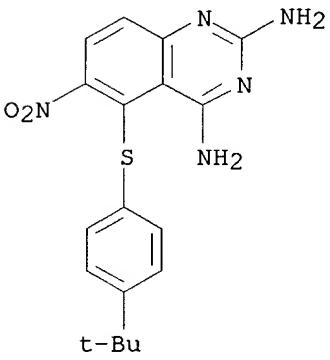
RN 168910-95-0 CAPLUS
CN 2,4-Quinazolinediamine, 5-[[4-(1,1-dimethylethyl)phenyl]thio]-6-ethoxy- (9CI) (CA INDEX NAME)



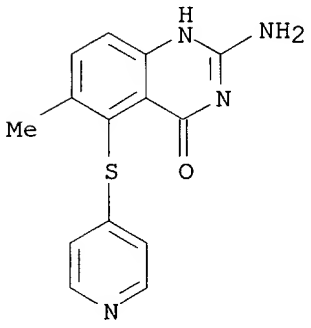
RN 168910-96-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-[[4-(1,1-dimethylethyl)phenyl]thio]-6-(2-methylpropoxy)- (9CI) (CA INDEX NAME)



IT **168910-29-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of (arylthio)quinazolinediamines as fungicides)
RN 168910-29-0 CAPLUS
CN 2,4-Quinazolinediamine, 5-[[4-(1,1-dimethylethyl)phenyl]thio]-6-nitro- (9CI) (CA INDEX NAME)

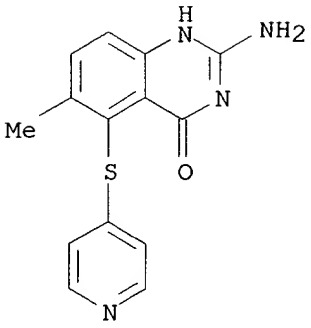


L14 ANSWER 39 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1995:691697 CAPLUS
DN 123:93099
TI Stability of AG337, a thymidylate synthase inhibitor, in PVC infusion bags
AU Thirucote, Ramachandran R.; Laskin, Paul; Tyle, Praveen
CS Pharmaceutial Development Dep., Agouron Pharmaceuticals, Inc., San Diego, CA, 92121, USA
SO Drug Dev. Ind. Pharm. (1995), 21(15), 1773-80
CODEN: DDIPD8; ISSN: 0363-9045
DT Journal
LA English
AB The stability of AG337, a selective thymidylate synthase inhibitor, in 5% dextrose in water (D5W) PVC infusion bags and sodium bicarbonate treated D5W infusion bags was studied at 30.degree.C for seven days. AG337 Soln. for Injection, 2% was dild. in D5W infusion bags to yield final AG337 concns. of 4 mg/mL, 1 mg/mL and 0.1 mg/mL. For the sodium bicarbonate treated D5W infusion bags, the final concns. of AG337 used were 4mg/mL, 1 mg/mL and 0.2 mg/mL. The bags were prepd. in triplicate and stored at 30.degree.C. At predetd. time intervals, each bag was visually examd. for presence of ppts. and samples were withdrawn for HPLC assay and pH testing. No pptn. was obsd. in any of the samples. The pH of the sodium bicarbonate treated D5W infusion bags remained const. throughout the study. The recovery of AG337 was greater than 93% in all samples tested. The recovery of Me and propylparaben, used as preservatives in the formulation, however, decreased over time probably due to adsorption in the PVC bags. This study demonstrated that AG337 was stable at 30.degree.C for up to seven days, in D5W infusion bags and in the presence of sodium bicarbonate treated D5W infusion bags.
IT **152946-68-4**, AG337
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stability of AG337, a thymidylate synthase inhibitor, in PVC infusion bags)
RN 152946-68-4 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)



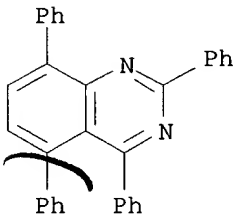
●2 HCl

L44 ANSWER 40 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1995:616040 CAPLUS
DN 123:25288
TI Mechanisms of acquired resistance to the quinazoline thymidylate synthase inhibitor ZD1694 (Tomudex) in one mouse and three human cell lines
AU Jackman, AL; Kelland, LR; Kimbell, R; Brown, M; Gibson, W; Aherne, GW; Hardcastle, A; Boyle, FT
CS Centre for Cancer Therapeutics, Institute of Cancer Research, Sutton/Surrey, SM2 5NG, UK
SO Br. J. Cancer (1995), 71(5), 914-24
CODEN: BJCAAI; ISSN: 0007-0920
DT Journal
LA English
AB Four cell lines, the mouse L1210 leukemia, the human W1L2 lymphoblastoid and two human ovarian (CH1 and 41M) cell lines, were made resistant to ZD1694 (Tomudex) by continual exposure to incremental doses of the drug. A 500-fold increase in thymidylate synthase (TS) activity is the primary mechanism of resistance to ZD1694 in the W1L2:RD1694 cell line, which is consequently highly cross-resistant to other folate-based TS inhibitors, including BW1843U89, LY231514 and AG337, but sensitive to antifolates with other enzyme targets. The CH1:RD1694 cell line is 14-fold resistant to ZD1694, largely accounted for by the 4.2-fold increase in TS activity. Cross-resistance was obsd. to other TS inhibitors, including 5-fluorodeoxyuridine (FdUrd). 41M:RD1694 cells, when exposed to 0.1 .mu.M [3H]ZD1694, accumulated .apprx.20-fold less 3H-labeled material over 24 h than the parental line. Data are consistent with this being the result of impaired transport of the drug via the reduced folate/methotrexate carrier. Resistance was therefore obsd. to methotrexate but not to CB3717, a compd. known to use this transport mechanism poorly. The mouse L1210:RD1694 cell line does not accumulate ZD1694 or methotrexate (MTX) polyglutamates. Folylpolyglutamate synthetase substrate activity (using ZD1694 as the substrate) was decreased to .apprx.13% of that obsd. in the parental line. Cross-resistance was found to those compds. known to be active through polyglutamation.
IT **152946-68-4**, AG337
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanisms of acquired resistance to quinazoline thymidylate synthase inhibitor ZD1694 (Tomudex) in tumor cell lines and cross resistance to other antitumor agents)
RN 152946-68-4 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)

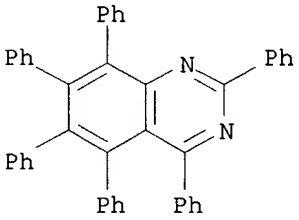


●2 HCl

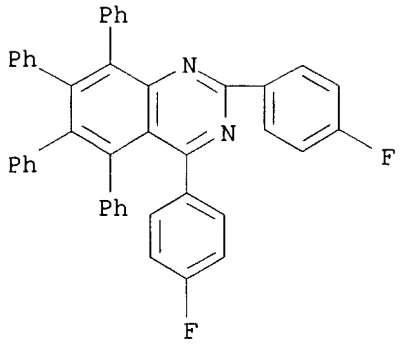
L[illegible] ANSWER 41 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1995:553881 CAPLUS
DN 123:33019
TI Thermal Rearrangement of a Phthalazine to a Quinazoline
AU Chan, Kwok P.; Hay, Allan S.
CS Department of Chemistry, McGill University, Montreal, PQ, H3A 2K6, Can.
SO J. Org. Chem. (1995), 60(10), 3131-4
CODEN: JOCEAH; ISSN: 0022-3263
DT Journal
LA English
AB The thermal rearrangement reaction of a phthalazine to its structural isomer, a quinazoline, was reported. Polyphenylated phthalazines at 360 .degree.C for 30 min gave the corresponding quinazolines in high yield. The less sterically crowded 1,4-bis(4-fluorophenyl)phthalazine gave only a low yield of 2,4-bis(4-fluorophenyl)quinazoline. X-ray crystallog. anal. on 2,4,5,8-tetraphenylquinazoline further confirmed our finding.
IT **163930-41-4P**, 2,4,5,8-Tetraphenylquinazoline **163930-42-5P** **163930-43-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(thermal rearrangement of phthalazine to quinazoline)
RN 163930-41-4 CAPLUS
CN Quinazoline, 2,4,5,8-tetraphenyl- (9CI) (CA INDEX NAME)



RN 163930-42-5 CAPLUS
CN Quinazoline, hexaphenyl- (9CI) (CA INDEX NAME)



RN 163930-43-6 CAPLUS
CN Quinazoline, 2,4-bis(4-fluorophenyl)-5,6,7,8-tetraphenyl- (9CI) (CA INDEX NAME)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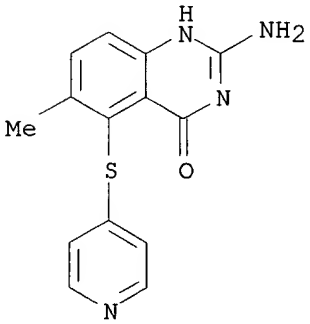
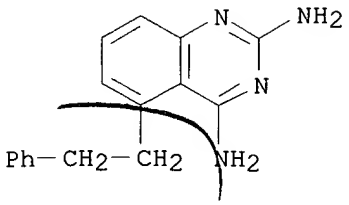
L14 ANSWER 42 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1995:519233 CAPLUS
DN 123:422
TI Evaluation of the mechanism of growth inhibition of AG337
AU Rhee, M. S.; Webber, S.; Galivan, J.
CS Division Molecular Medicine, Wadsworth Center, Albany, NY, 12201-0509, USA
SO Cell. Pharmacol. (1995), 2(2), 97-101
CODEN: CEPHEG; ISSN: 1351-3214
DT Journal
LA English
AB AG337 (3,4-dihydro-2-amino-6-methyl-4-oxo-5(4-pyridylthio)quinazoline dihydrochloride) is an inhibitor of thymidylate synthase (TS) that was synthesized based upon the x-ray crystallog. structure of the enzyme. This compd. was examd. in a rat hepatoma cell line in culture to det. whether the inhibition of TS was its basis of cytotoxicity. The use of various antifolate resistant cells demonstrate that it does not enter cells by the reduced folate carrier, is not polyglutamylated, does not inhibit dihydrofolate reductase, and that TS amplified cells are strongly resistant. Several other lines of experimentation provide evidence for the involvement of TS as the target site. AG337 is protected against by thymidine and not hypoxanthine and it inhibits deoxyuridine incorporation and not that of glycine. Cell cycle anal. demonstrates S phase arrest which is prevented by thymidine. Folinic acid failed to protect cells against AG337, further suggesting that folate transport and polyglutamylation are not components of its inhibitory properties. AG337 had little effect on confluent cultures, which is consistent with the lack of effect of antifolates on H35 cells and different from AG331, an earlier rationally designed TS inhibitor that does not have TS as the cellular site of action in this system. These results demonstrate that the primary target of AG337 in H35 hepatoma cells, at concns. up to ten fold greater than the IC50, is TS.
IT **152946-68-4**, AG 337
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(AG337 inhibition of thymidylate synthase in relation to antitumor activity)
RN 152946-68-4 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)

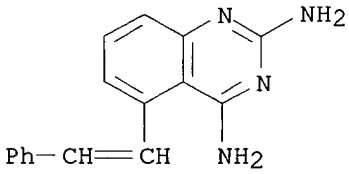


2 HCl

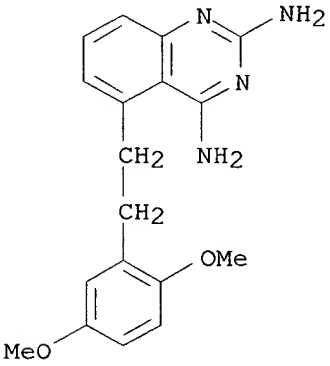
L1 ANSWER 43 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1995:380746 CAPLUS
DN 122:150852
TI 2,4-Diamino-5-substituted-quinazolines as Inhibitors of a Human Dihydrofolate Reductase with a Site-Directed Mutation at Position 22 and of the Dihydrofolate Reductases from Pneumocystis carinii and Toxoplasma gondii
AU Rosowsky, Andre; Mota, Clara E.; Queener, Sherry F.; Waltham, Mark; Ercikan-Abali, Emine; Bertino, Joseph R.
CS Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, 02115, USA
SO Journal of Medicinal Chemistry (1995), 38(5), 745-52
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 122:150852
AB 2,4-Diaminoquinazoline antifolates with a lipophilic side chain at the 5-position, and in one case with a classical (p-aminobenzoyl)-L-glutamate side chain, were synthesized as potentially selective inhibitors of a site-directed mutant of human dihydrofolate reductase (DHFR) contg. phenylalanine instead of leucine at position 22. This mutant enzyme is approx. 100-fold more resistant than native enzyme to the classical antifolate methotrexate (MTX), yet shows minimal cross resistance to the nonclassical antifolates piritrexim (PTX) and trimetrexate (TMQ). Although they were much less potent than trimetrexate and piritrexim, the lipophilic 5-substituted analogs were all found to bind approx. 10 times better to the mutant DHFR than to the wild-type enzyme. The potency of the analog with a classical (p-aminobenzoyl)-L-glutamate side chain was similarly diminished in comparison with MTX, but the difference in its binding affinity to the two DHFR species was only 5-fold. Thus, by making subtle structural changes in the antifolate mol., it may be possible to attack resistance due to mutational alterations in the active site of the target enzyme. Also, to test the hypothesis that DHFR from Pneumocystis carinii and Toxoplasma gondii may have a less sterically restrictive active site than the enzyme from mammalian cells, inhibition assays using several of the lipophilic analogs in the series were done against the P. carinii and T. gondii reductases in comparison with the enzyme from rat liver. In contrast to their preferential binding to mutant vs. wild-type human DHFR, binding of these analogs to the P. carinii and T. gondii enzymes was weaker than binding to rat enzyme. It thus appears that, if the active site of the DHFR from these parasites is less sterically restrictive than the active site of the mammalian enzyme, this difference cannot be successfully exploited by moving the side chain from the 6-position to the 5-position.
IT **123242-02-4P 161201-10-1P 161201-12-3P 161201-14-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(diamino-substituted-quinazolines as inhibitors of human dihydrofolate reductase with site-directed mutation at position 22 and of dihydrofolate reductases from Pneumocystis carinii and Toxoplasma gondii)
RN 123242-02-4 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-phenylethyl)- (9CI) (CA INDEX NAME)



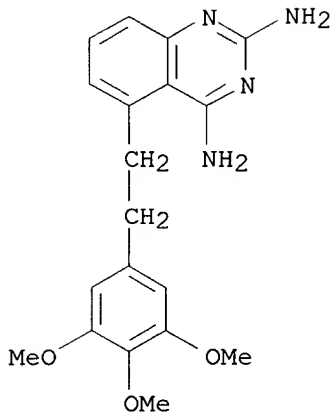
RN 161201-10-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-phenylethenyl)- (9CI) (CA INDEX NAME)



RN 161201-12-3 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2,5-dimethoxyphenyl)ethyl]- (9CI) (CA INDEX NAME)



RN 161201-14-5 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(3,4,5-trimethoxyphenyl)ethyl]- (9CI) (CA INDEX NAME)


N
NH2
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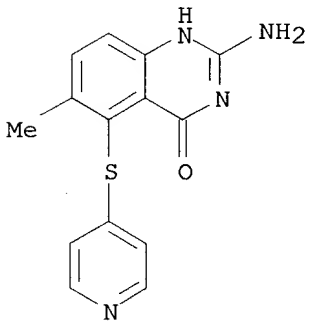
CH2
NH2
CH2
MeO
OMe
OMe

L14 ANSWER 44 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1995:226507 CAPLUS
DN 123:17739
TI Parenteral product development of AG337, a thymidylate synthase inhibitor
AU Thirucote, Ramachandran; Laskin, Paul; Chiang, Chin Chin; Tyle, Praveen
CS Pharm. Development Dep., Agouron Pharm., Inc., San Diego, CA, 92121, USA
SO Eur. J. Pharm. Biopharm. (1994), 40(5), 271-6
CODEN: EJPBEL
DT Journal
LA English
AB The title anticancer drug (I) a quinazolinone deriv., was developed as a parenteral soln. contg. 2, 0.18 and 0.02, and 50% of I, methyl- and propylparabens, and propylene glycol in NaOAc buffer, resp. The soln. was maintained at pH 3.0-5.0 and a kinetic study under accelerated conditions (80.degree.) indicated soln. stability was independent of pH between 3-7, with a max. stability at pH 5.0. Acetate buffers were added to maintain pH at .gtoreq.3.0 and propylene glycol was added to maintain I soly. at 20 mg mL-1. The 9:1 combination of methyl- and propylparabens was selected as antimicrobial preservation system. Of various filter membranes tested for their compatibility for aseptic filtration, a 0.22 .mu.m poly(vinylidenedifluoride) membrane was the most suitable. Autoclaving with moist heat at 121.degree. was more suitable than .gamma.- or electron beam irradn. for sterilization. The formulation was compatible with infusion fluids in PVC infusion bags such as a 5% dextrose soln.
IT **152946-68-4**, AG 337
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(parenteral formulations of AG337 thymidylate synthase inhibitor)
RN 152946-68-4 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 45 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1994:695126 CAPLUS
DN 121:295126
TI Preparation of insecticidal substituted 2,4-diaminoquinazolines.
IN Henrie, Robert Neil, II; Peake, Clinton Joseph; Cullen, Thomas Gerard; Lew, Albert C.; Chaguturu, Munirathnam Krishnappa; Ray, Partha Sarathi
PA FMC Corp., USA
SO PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9418980	A1	19940901	WO 1994-US1658	19940217
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ZA 9401038	A	19940825	ZA 1994-1038	19940215
AU 9462986	A1	19940914	AU 1994-62986	19940217
EP 684824	A1	19951206	EP 1994-910694	19940217
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI				

PRAI US 1993-19389 19930218
US 1993-149491 19931109
WO 1994-US1658 19940217
OS MARPAT 121:295126
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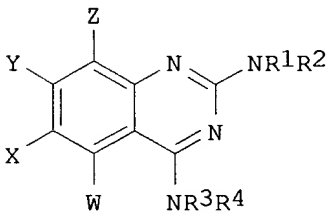


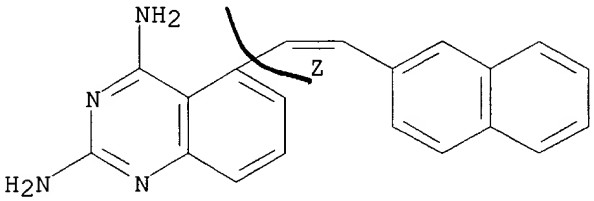
I

AB The title compds. I [R1= H, alkyl; R2,R3= R1, alkylcarbonyl, alkoxycarbonyl; R4 = H; R1R2= alkylenoxyalkylene; W, Y, Z = H,, halo, (halo)alkyl, (halo)alkoxy, (un)substituted thienyl or aroyl, etc.; X = H, halo, (halo)alkyl, NHCH2C6H4CO2H-4, etc.] are prepd. as insecticides. 2-Amino-6-methyl-5-[3,5-di(trifluoromethyl)phenyl]benzonitrile (prepn. given) was reacted with chloroformamidine-HCl (prepn. given) in diglyme, to yield 2,4-diamino-6-methyl-5-[3,5-di(trifluoromethyl)phenyl]quinazoline (II). Diets contg. 4% II were lethal to the tobacco budworm (Heliothis virescens).

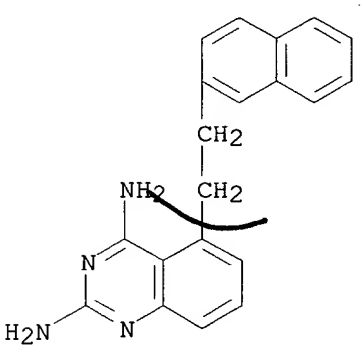
IT **50828-08-5P 50828-09-6P 50828-12-1P**
50828-13-2P 50828-17-6P 50828-18-7P
50828-19-8P 159018-80-1P 159018-94-7P
159019-02-0P 159019-13-3P
RL: AGR (Agricultural use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of insecticidal diaminoquinazolines)

RN 50828-08-5 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethenyl]-, (Z)- (9CI) (CA INDEX NAME)

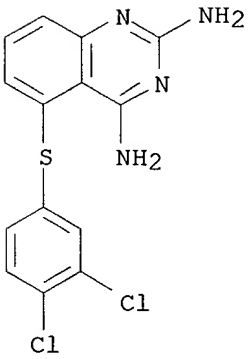
Double bond geometry as shown.



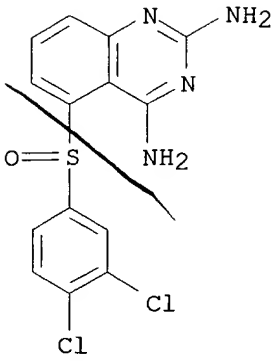
RN 50828-09-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethyl]- (9CI) (CA INDEX NAME)



RN 50828-12-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)thio]- (9CI) (CA INDEX NAME)

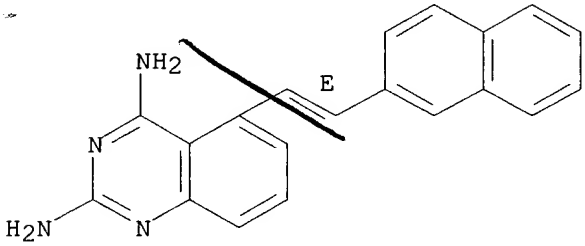


RN 50828-13-2 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)sulfinyl]- (9CI) (CA INDEX NAME)

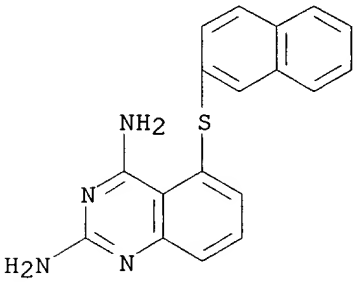


RN 50828-17-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

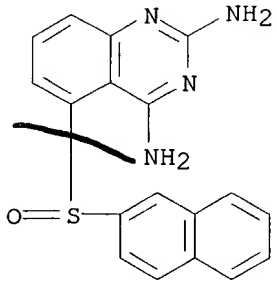
Double bond geometry as shown.



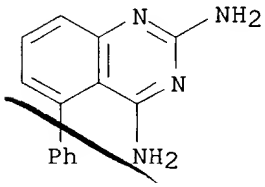
RN 50828-18-7 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)



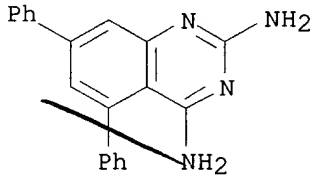
RN 50828-19-8 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylsulfinyl)- (9CI) (CA INDEX NAME)



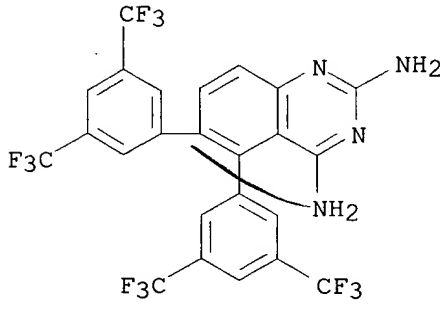
RN 159018-80-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-phenyl- (9CI) (CA INDEX NAME)



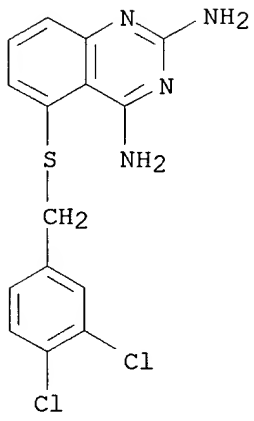
RN 159018-94-7 CAPLUS
CN 2,4-Quinazolinediamine, 5,7-diphenyl- (9CI) (CA INDEX NAME)



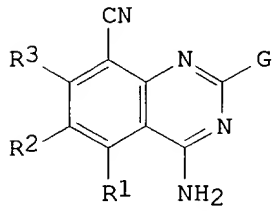
RN 159019-02-0 CAPLUS
CN 2,4-Quinazolinediamine, 5,6-bis[3,5-bis(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 159019-13-3 CAPLUS
CN 2,4-Quinazolinediamine, 5-[[(3,4-dichlorophenyl)methyl]thio]- (9CI) (CA INDEX NAME)

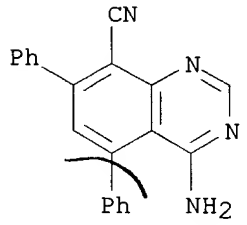

N
NH2
N
S
NH2
CH2
Cl
Cl

L14 ANSWER 46 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1994:191659 CAPLUS
DN 120:191659
TI Synthesis of 4-amino-8-cyanoquinazolines from enones and enals
AU Victory, Pedro; Borrell, Jose I.; Vidal-Ferran, Anton; Montenegro, Elvira; Jimeno, M. Luisa
CS Dep. Quim. Org., CETS, Barcelona, E-08017, Spain
SO Heterocycles (1993), 36(10), 2273-80
CODEN: HTCYAM; ISSN: 0385-5414
DT Journal
LA English
GI

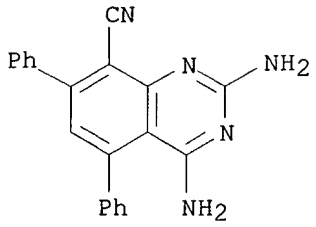


I

AB The treatment in a Na methoxide/MeOH soln. of .alpha.,.beta.-unsatd. enones or aldehydes with propanedinitrile in a 1:2 molar ratio led to 2-aminobenzene-1,3-dicarbonitriles. These compds. afforded 4-amino-8-cyanoquinazolines I (R1-R3 = H, Ph, Me; G = H, NH2) by reaction with formamide or guanidine.
IT **153492-27-4P**, 4-Amino-5,7-diphenyl-8-quinazolinecarbonitrile
153492-29-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 153492-27-4 CAPLUS
CN 8-Quinazolinecarbonitrile, 4-amino-5,7-diphenyl- (9CI) (CA INDEX NAME)



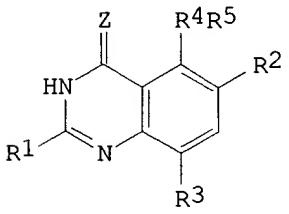
RN 153492-29-6 CAPLUS
CN 8-Quinazolinecarbonitrile, 2,4-diamino-5,7-diphenyl- (9CI) (CA INDEX NAME)


CN
Ph
N
NH2
N
Ph
NH2

L14 ANSWER 47 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1994:164214 CAPLUS
DN 120:164214
TI Quinazoline inhibitors of thymidylate synthase
IN Webber, Stephen E.; Bleckman, Ted M.; Attard, John; Jones, Terence R.; Varney, Michael D.
PA Agouron Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9320055	A1	19931014	WO 1993-US2636	19930326
	W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5430148	A	19950704	US 1992-861030	19920331
	AU 9339664	A1	19931108	AU 1993-39664	19930326
	AU 681075	B2	19970821		
	EP 637300	A1	19950208	EP 1993-909143	19930326
	EP 637300	B1	20010905		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 07505395	T2	19950615	JP 1993-517514	19930326
	JP 3272357	B2	20020408		
	HU 68580	A2	19950628	HU 1994-2799	19930326
	RU 2135481	C1	19990827	RU 1994-45251	19930326
	AT 205197	E	20010915	AT 1993-909143	19930326
	ES 2162818	T3	20020116	ES 1993-909143	19930326
	FI 9404525	A	19940929	FI 1994-4525	19940929
	NO 9403629	A	19940929	NO 1994-3629	19940929
	US 5707992	A	19980113	US 1995-418415	19950407
	US 5885996	A	19990323	US 1997-923117	19970904
PRAI	US 1992-861030	A	19920331		
	WO 1993-US2636	A	19930326		
	US 1995-418415	A3	19950407		

OS MARPAT 120:164214
GI



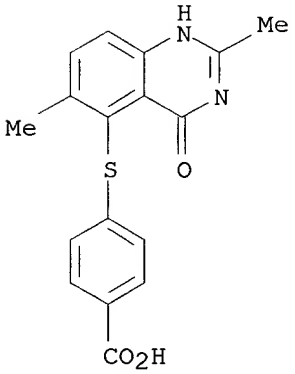
I

AB The title compds. I [R1 = H, halogen, alkyl, OH, alkoxy, aryloxy, heteroaryloxy, alkylthio, (un)substituted NH2, etc.; R2, R3 = H, halogen, alkyl, cycloalkyl, OH, alkoxy, alkylthio, (un)substituted NH2, CN,

(un)substituted CO2H, etc.; R4 = O, S, SO, SO2, NH, alkyl-substituted N, CH2, CHOH, etc.; R5 = (un)substituted aryl or heteroaryl; Z = O, S], which inhibit the enzyme thymidylate synthase and which possess antitumor activity, antibiotic activity, antifungal activity, etc., are prepd. Thus, 5-benzoyl-2-methyl-3-[2'-(trimethylsilyl)ethoxymethyl]quinazolin-4-one was deprotected with HCl, neutralized with NaHCO3, and condensed with PhLi, producing I [R1 = Me, R2 = R3 = H, R4 = C(OH)Ph, R5 = Ph, Z = O] (II). II demonstrated Ki against E. coli of >10 .mu.M and demonstrated 50% inhibitory concn. against L12120 murine leukemia cell culture of 2.3 .mu.M.

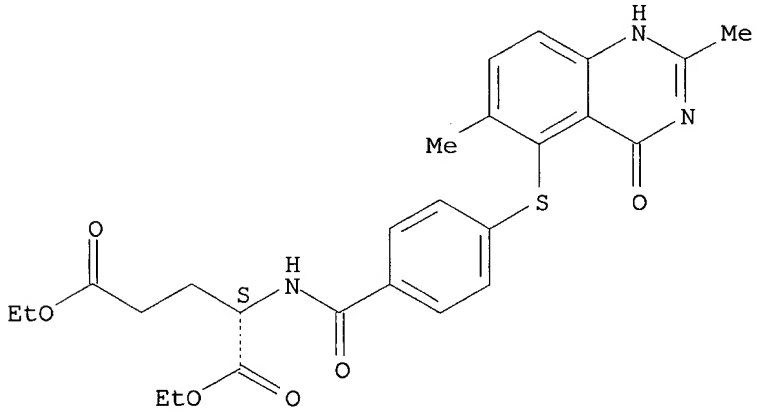
IT **147149-69-7P 147150-02-5P 152946-39-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of quinazoline thymidylate synthase inhibitors)

RN 147149-69-7 CAPLUS
CN Benzoic acid, 4-[(1,4-dihydro-2,6-dimethyl-4-oxo-5-quinazolinyl)thio]- (9CI) (CA INDEX NAME)



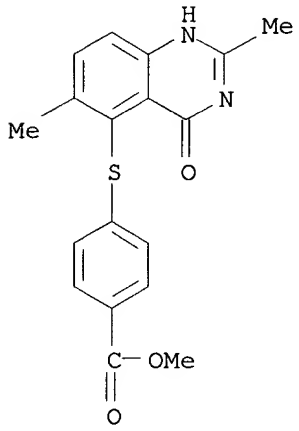
RN 147150-02-5 CAPLUS
CN L-Glutamic acid, N-[4-[(1,4-dihydro-2,6-dimethyl-4-oxo-5-quinazolinyl)thio]benzoyl]-, diethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 152946-39-9 CAPLUS

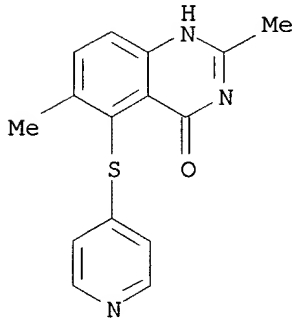
CN Benzoic acid, 4-[(1,4-dihydro-2,6-dimethyl-4-oxo-5-quinazolinyl)thio]-, methyl ester (9CI) (CA INDEX NAME)



IT **147149-63-1P 147149-65-3P 147149-66-4P**
147149-72-2P 147149-73-3P 147149-74-4P
147149-75-5P 147149-76-6P 147149-78-8P
147149-81-3P 152946-43-5P 152946-46-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and thymidylate synthase inhibitory activity of)

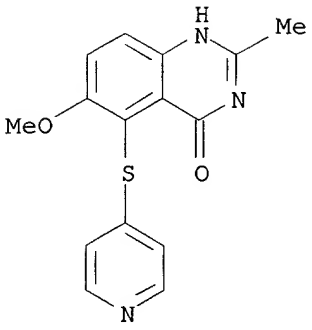
RN 147149-63-1 CAPLUS

CN 4(1H)-Quinazolinone, 2,6-dimethyl-5-(4-pyridinylthio)- (9CI) (CA INDEX NAME)

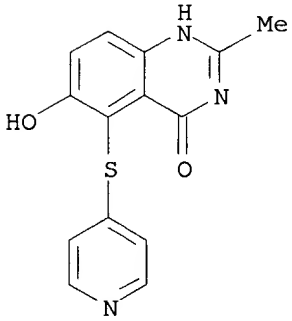


RN 147149-65-3 CAPLUS

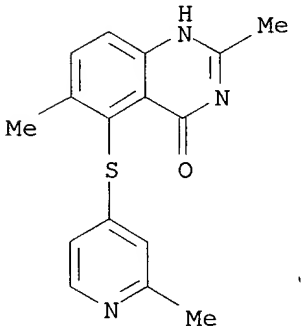
CN 4(1H)-Quinazolinone, 6-methoxy-2-methyl-5-(4-pyridinylthio)- (9CI) (CA INDEX NAME)



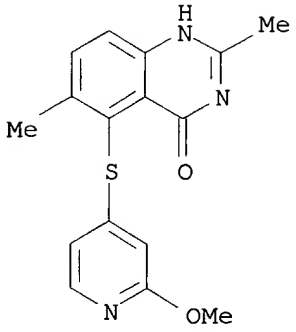
RN 147149-66-4 CAPLUS
CN 4(1H)-Quinazolinone, 6-hydroxy-2-methyl-5-(4-pyridinylthio)- (9CI) (CA INDEX NAME)



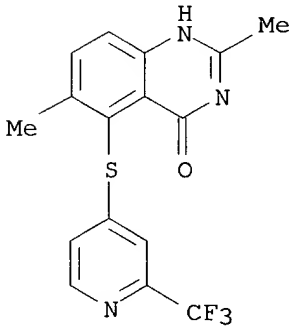
RN 147149-72-2 CAPLUS
CN 4(1H)-Quinazolinone, 2,6-dimethyl-5-[(2-methyl-4-pyridinyl)thio]- (9CI) (CA INDEX NAME)



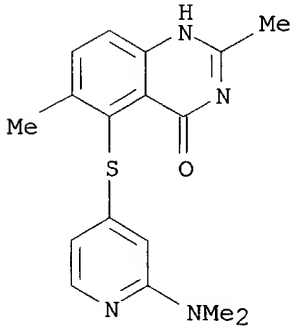
RN 147149-73-3 CAPLUS
CN 4(1H)-Quinazolinone, 5-[(2-methoxy-4-pyridinyl)thio]-2,6-dimethyl- (9CI) (CA INDEX NAME)



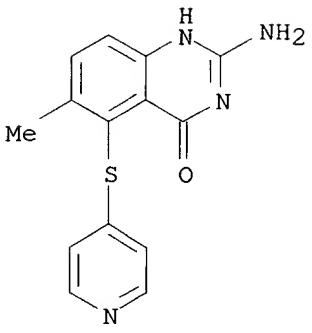
RN 147149-74-4 CAPLUS
CN 4(1H)-Quinazolinone, 2,6-dimethyl-5-[[2-(trifluoromethyl)-4-pyridinyl]thio]- (9CI) (CA INDEX NAME)



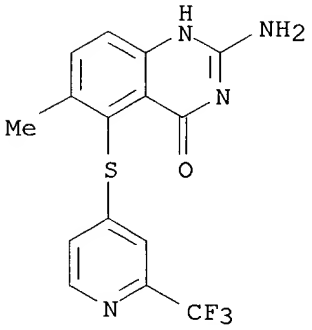
RN 147149-75-5 CAPLUS
CN 4(1H)-Quinazolinone, 5-[[2-(dimethylamino)-4-pyridinyl]thio]-2,6-dimethyl- (9CI) (CA INDEX NAME)



RN 147149-76-6 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)- (9CI) (CA INDEX NAME)

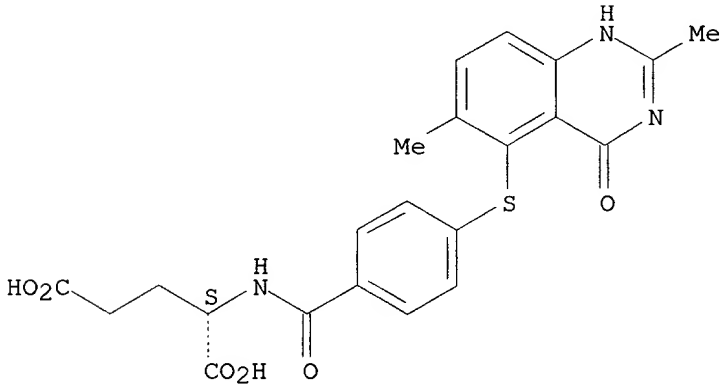


RN 147149-78-8 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-[[2-(trifluoromethyl)-4-pyridinyl]thio]- (9CI) (CA INDEX NAME)

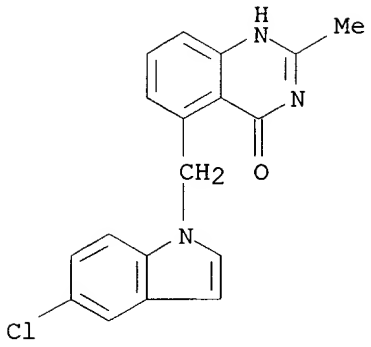


RN 147149-81-3 CAPLUS
CN L-Glutamic acid, N-[4-[(1,4-dihydro-2,6-dimethyl-4-oxo-5-quinazolinyl)thio]benzoyl]- (9CI) (CA INDEX NAME)

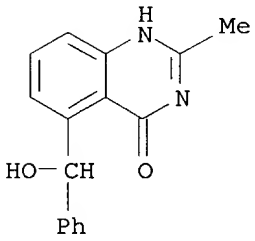
Absolute stereochemistry.



RN 152946-43-5 CAPLUS
CN 4(1H)-Quinazolinone, 5-[(5-chloro-1H-indol-1-yl)methyl]-2-methyl- (9CI) (CA INDEX NAME)

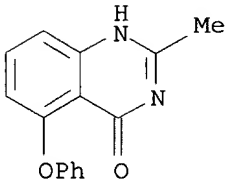


RN 152946-46-8 CAPLUS
CN 4(1H)-Quinazolinone, 5-(hydroxyphenylmethyl)-2-methyl- (9CI) (CA INDEX NAME)

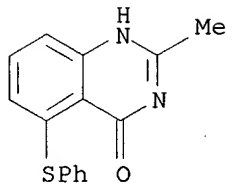


IT **147149-59-5 147149-60-8 147149-61-9**
147149-62-0 147149-64-2 147149-65-3
147149-67-5 147149-68-6 147149-69-7
147149-70-0 147149-71-1 147149-75-5
147149-80-2 147149-81-3 152946-50-4
152946-52-6 152946-54-8 152946-55-9
152946-56-0 152946-57-1 152946-58-2
152946-59-3 152946-60-6 152946-61-7
152946-62-8 152946-63-9 152946-64-0
152946-65-1 152946-66-2 152946-67-3
152946-68-4 152946-69-5
RL: RCT (Reactant)
(thymidylate synthase inhibitory activity of)

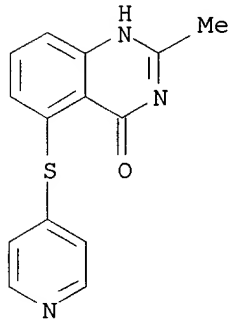
RN 147149-59-5 CAPLUS
CN 4(1H)-Quinazolinone, 2-methyl-5-phenoxy- (9CI) (CA INDEX NAME)



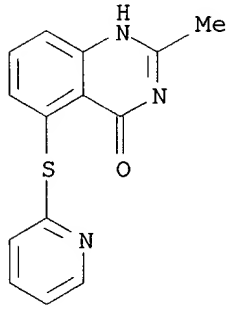
RN 147149-60-8 CAPLUS
CN 4(1H)-Quinazolinone, 2-methyl-5-(phenylthio)- (9CI) (CA INDEX NAME)



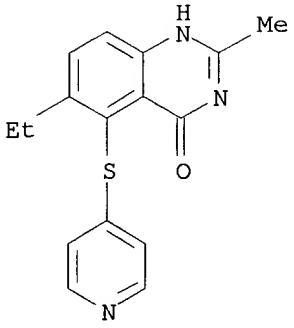
RN 147149-61-9 CAPLUS
CN 4(1H)-Quinazolinone, 2-methyl-5-(4-pyridinylthio)- (9CI) (CA INDEX NAME)



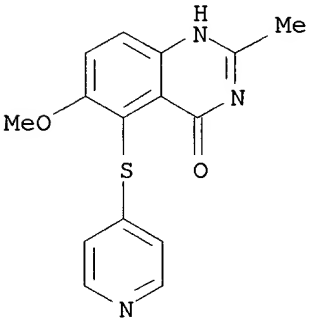
RN 147149-62-0 CAPLUS
CN 4(1H)-Quinazolinone, 2-methyl-5-(2-pyridinylthio)- (9CI) (CA INDEX NAME)



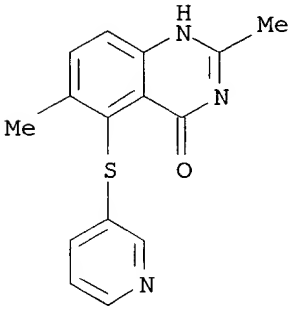
RN 147149-64-2 CAPLUS
CN 4(1H)-Quinazolinone, 6-ethyl-2-methyl-5-(4-pyridinylthio)- (9CI) (CA INDEX NAME)



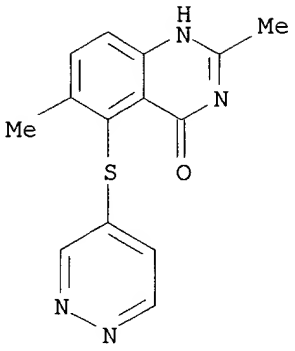
RN 147149-65-3 CAPLUS
CN 4(1H)-Quinazolinone, 6-methoxy-2-methyl-5-(4-pyridinylthio)- (9CI) (CA INDEX NAME)



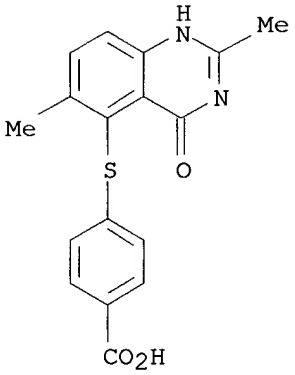
RN 147149-67-5 CAPLUS
CN 4(1H)-Quinazolinone, 2,6-dimethyl-5-(3-pyridinylthio)- (9CI) (CA INDEX NAME)



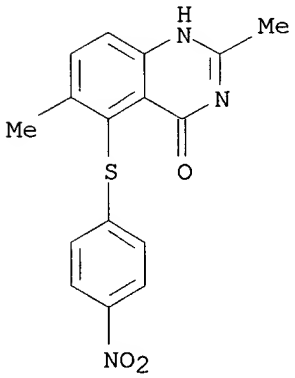
RN 147149-68-6 CAPLUS
CN 4(1H)-Quinazolinone, 2,6-dimethyl-5-(4-pyridazinylthio)- (9CI) (CA INDEX NAME)



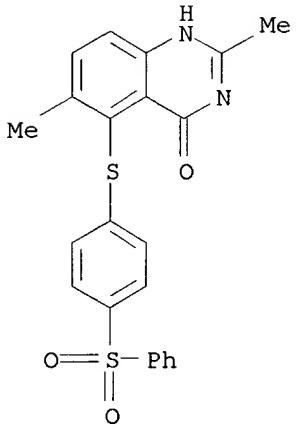
RN 147149-69-7 CAPLUS
CN Benzoic acid, 4-[(1,4-dihydro-2,6-dimethyl-4-oxo-5-quinazolinyl)thio]- (9CI) (CA INDEX NAME)



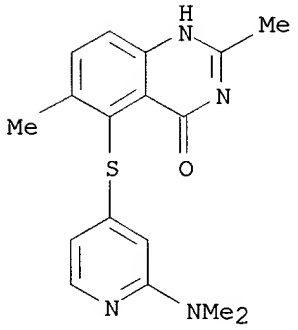
RN 147149-70-0 CAPLUS
CN 4(1H)-Quinazolinone, 2,6-dimethyl-5-[(4-nitrophenyl)thio]- (9CI) (CA INDEX NAME)



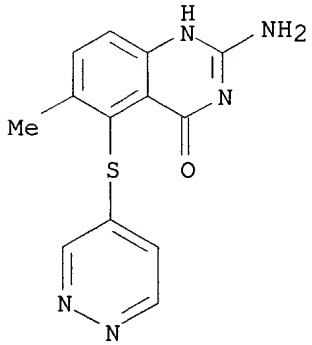
RN 147149-71-1 CAPLUS
CN 4(1H)-Quinazolinone, 2,6-dimethyl-5-[[4-(phenylsulfonyl)phenyl]thio]- (9CI) (CA INDEX NAME)



RN 147149-75-5 CAPLUS
CN 4(1H)-Quinazolinone, 5-[[2-(dimethylamino)-4-pyridinyl]thio]-2,6-dimethyl- (9CI) (CA INDEX NAME)



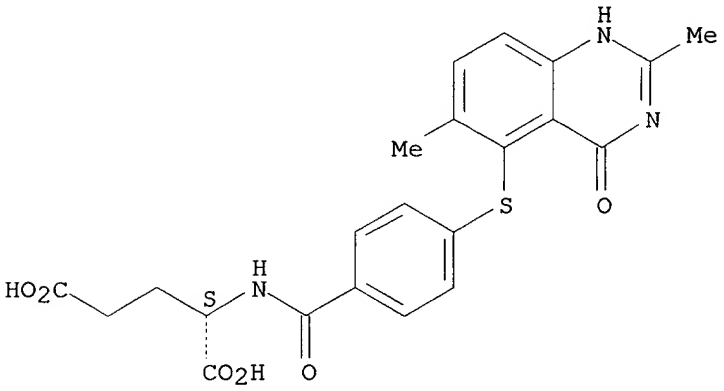
RN 147149-80-2 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridazinylthio)- (9CI) (CA INDEX NAME)



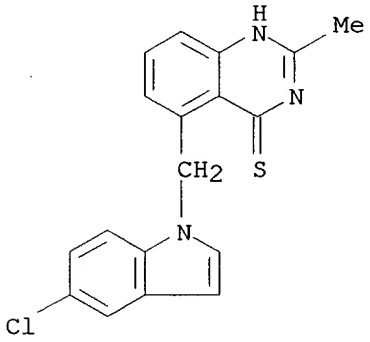
RN 147149-81-3 CAPLUS

CN L-Glutamic acid, N-[4-[(1,4-dihydro-2,6-dimethyl-4-oxo-5-quinazolinyl)thio]benzoyl]- (9CI) (CA INDEX NAME)

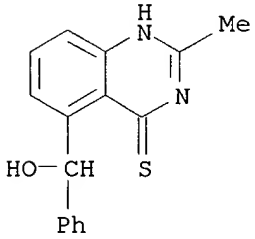
Absolute stereochemistry.



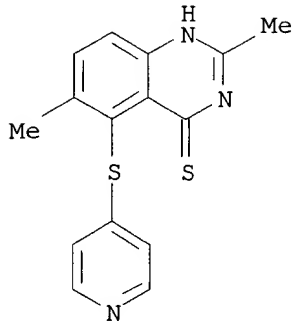
RN 152946-50-4 CAPLUS
CN 4(1H)-Quinazolinethione, 5-[(5-chloro-1H-indol-1-yl)methyl]-2-methyl- (9CI) (CA INDEX NAME)



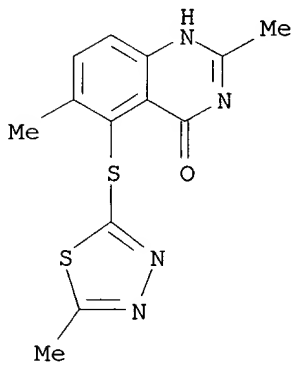
RN 152946-52-6 CAPLUS
CN 4(1H)-Quinazolinethione, 5-(hydroxyphenylmethyl)-2-methyl- (9CI) (CA INDEX NAME)



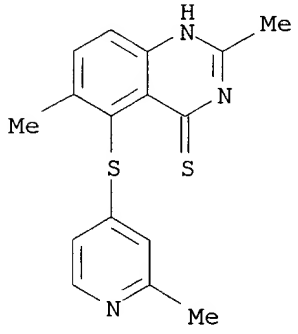
RN 152946-54-8 CAPLUS
CN 4(1H)-Quinazolinethione, 2,6-dimethyl-5-(4-pyridinylthio)- (9CI) (CA INDEX NAME)



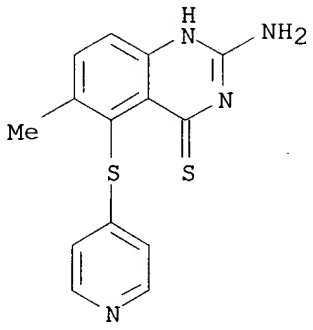
RN 152946-55-9 CAPLUS
CN 4(1H)-Quinazolinone, 2,6-dimethyl-5-[(5-methyl-1,3,4-thiadiazol-2-yl)thio]- (9CI) (CA INDEX NAME)



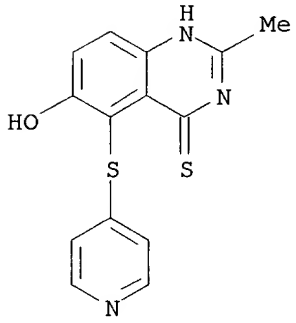
RN 152946-56-0 CAPLUS
CN 4(1H)-Quinazolinethione, 2,6-dimethyl-5-[(2-methyl-4-pyridinyl)thio]- (9CI) (CA INDEX NAME)



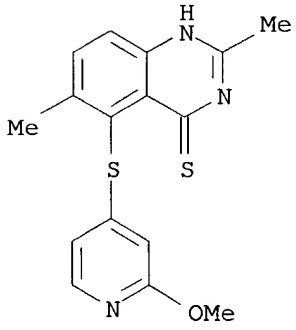
RN 152946-57-1 CAPLUS
CN 4(1H)-Quinazolinethione, 2-amino-6-methyl-5-(4-pyridinylthio)- (9CI) (CA INDEX NAME)



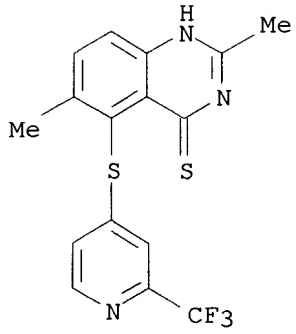
RN 152946-58-2 CAPLUS
CN 4(1H)-Quinazolinethione, 6-hydroxy-2-methyl-5-(4-pyridinylthio)- (9CI) (CA INDEX NAME)



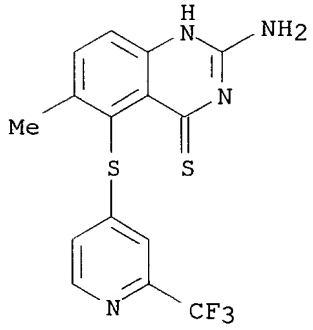
RN 152946-59-3 CAPLUS
CN 4(1H)-Quinazolinethione, 5-[(2-methoxy-4-pyridinyl)thio]-2,6-dimethyl- (9CI) (CA INDEX NAME)



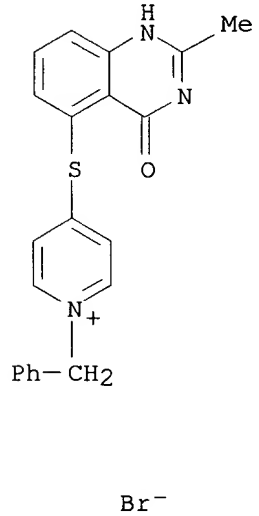
RN 152946-60-6 CAPLUS
CN 4(1H)-Quinazolinethione, 2,6-dimethyl-5-[[2-(trifluoromethyl)-4-pyridinyl]thio]- (9CI) (CA INDEX NAME)



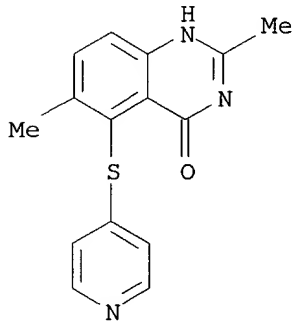
RN 152946-61-7 CAPLUS
CN 4(1H)-Quinazolinethione, 2-amino-6-methyl-5-[[2-(trifluoromethyl)-4-pyridinyl]thio]- (9CI) (CA INDEX NAME)



RN 152946-62-8 CAPLUS
CN Pyridinium, 4-[(1,4-dihydro-2-methyl-4-oxo-5-quinazolinyl)thio]-1-(phenylmethyl)-, bromide (9CI) (CA INDEX NAME)

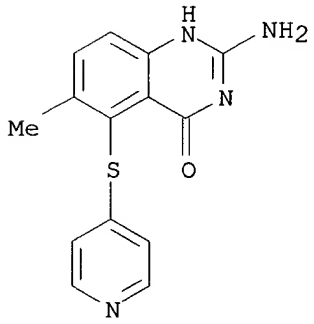


RN 152946-63-9 CAPLUS
CN 4(1H)-Quinazolinone, 2,6-dimethyl-5-(4-pyridinylthio)-, monohydrochloride (9CI) (CA INDEX NAME)



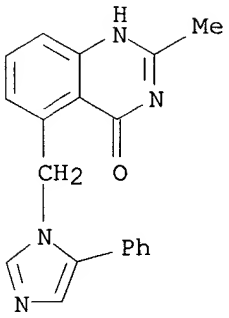
● HCl

RN 152946-64-0 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, monohydrochloride (9CI) (CA INDEX NAME)

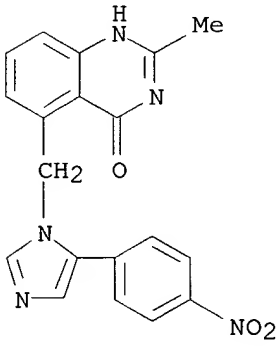


● HCl

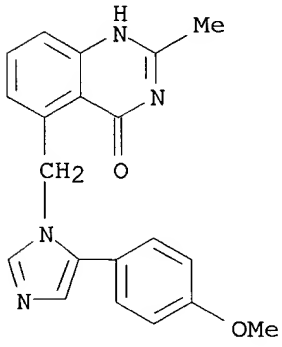
RN 152946-65-1 CAPLUS
CN 4(1H)-Quinazolinone, 2-methyl-5-[(5-phenyl-1H-imidazol-1-yl)methyl]- (9CI) (CA INDEX NAME)



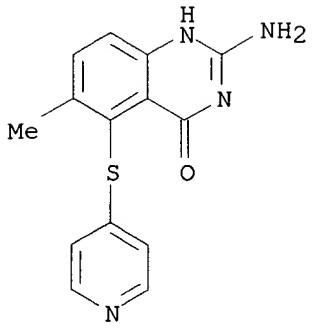
RN 152946-66-2 CAPLUS
CN 4(1H)-Quinazolinone, 2-methyl-5-[[5-(4-nitrophenyl)-1H-imidazol-1-yl]methyl]- (9CI) (CA INDEX NAME)



RN 152946-67-3 CAPLUS
CN 4(1H)-Quinazolinone, 5-[[5-(4-methoxyphenyl)-1H-imidazol-1-yl]methyl]-2-methyl- (9CI) (CA INDEX NAME)

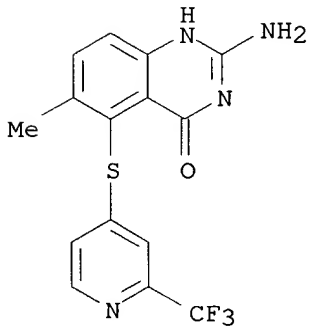


RN 152946-68-4 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 152946-69-5 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-[[2-(trifluoromethyl)-4-pyridinyl]thio]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 48 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1993:649710 CAPLUS
DN 119:249710
TI .alpha.-substituted benzenemethanamine antiviral derivatives
IN Janssen, Marcel August Constant; Van Daele, Georges Henri Paul; Bosmans, Jean Paul Rene Marie Andre; Van den Keybus, Frans Maria Alfons; Nuyens, Karin Josepha Malvina Maria; Janssen, Paul Adriaan Jan
PA Janssen Pharmaceutica N.V., Belg.
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9313052	A1	19930708	WO 1992-EP2995	19921222
	W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, NZ, PL, PT, RO, RU, SD, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
	AU 9332581	A1	19930728	AU 1993-32581	19921222
	AU 664874	B2	19951207		
	EP 620809	A1	19941026	EP 1993-901721	19921222
	EP 620809	B1	19970305		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	HU 67030	A2	19950130	HU 1994-1381	19921222
	JP 07502524	T2	19950316	JP 1992-511437	19921222
	AT 149484	E	19970315	AT 1993-901721	19921222
	CN 1073936	A	19930707	CN 1992-115152	19921229
	CN 1033451	B	19961204		
	ZA 9210079	A	19940629	ZA 1992-10079	19921229
	IL 104258	A1	19970415	IL 1992-104258	19921229
	US 5407961	A	19950418	US 1994-240735	19940512
	FI 9403120	A	19940629	FI 1994-3120	19940629
	NO 9402481	A	19940630	NO 1994-2481	19940630
	US 5480912	A	19960102	US 1995-400218	19950307
PRAI	EP 1991-203430		19911230		
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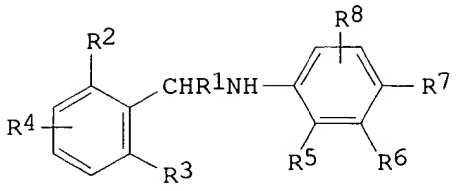
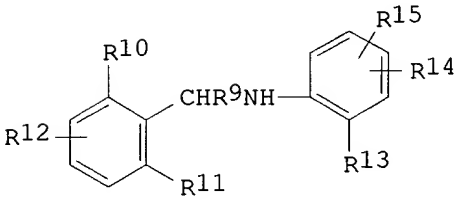
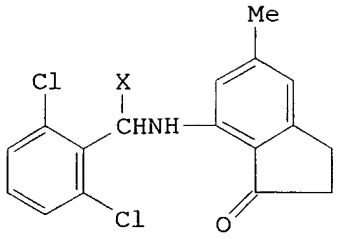
OS MARPAT 119:249710
GI



I



II



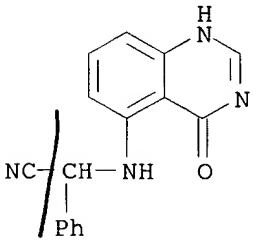
III

AB The title compds. I [R1 = CF3, methylcarbonyl, C3-6 cycloalkyl, (un)substituted carbonylamino or thiocarbonylamino; R2, R3 = halogen, methyl; R4 = H, OH, halogen, NO2, CF3; R8 = H, C1-6 alkoxy, C1-6 alkyl, halogen, NO2, aminocarbonyl, etc.; R7 = H in which case R5R6 = (un)substituted bivalent radical; R6R7 = (un)substituted (CH2)m in which case R5 = H, C1-6 alkoxy, C1-6 alkyl, halogen, NO2, etc.; m = 3,4] or II (R9 = CF3, MeCO, C3-6 cycloalkyl, etc.; R10, R11 = halogen, methyl; R12 = H, HO, halogen, NO2, CF3; R13 = C1-6 alkoxy, NO2, F3CO, 2,2,2-trifluoroethoxy, etc.; R14, R15 = H, halogen, C1-4 alkyl, NO2, C1-4 alkoxy, CF3), useful in the treatment of retroviruses (e.g., HIV-1), are prepd. and I- and II-contg. pharmaceutical formulations are presented. Thus, benzenemethanamine III (X = CN) was oxidized in the presence of formic acid and HCl, producing III (X = CONH2) (IV) (m.p. 249.5.degree.). Product IV demonstrated 50% protection concn. against HIV-1-transformed T4 cells of 0.0038 .mu.g/mL.

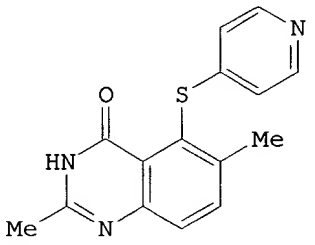
IT **150806-09-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of benzenemethanamine antiviral agents)

RN 150806-09-0 CAPLUS

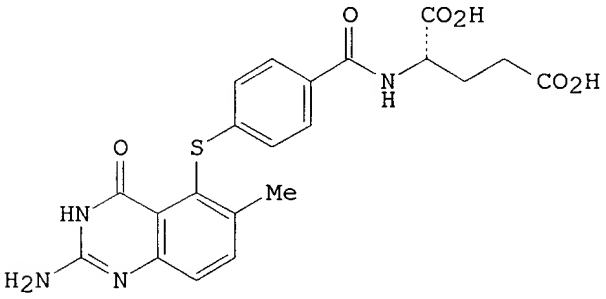
CN Benzeneacetonitrile, .alpha.-[(1,4-dihydro-4-oxo-5-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



L14 ANSWER 49 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1993:233990 CAPLUS
DN 118:233990
TI Design of thymidylate synthase inhibitors using protein crystal structures: the synthesis and biological evaluation of a novel class of 5-substituted quinazolinones
AU Webber, Stephen E.; Bleckman, Ted M.; Attard, John; Deal, Judith G.; Kathardekar, Vinit; Welsh, Katherine M.; Webber, Stephanie; Janson, Cheryl A.; Matthews, David A.; et al.
CS Agouron Pharm., Inc., San Diego, CA, 92121, USA
SO J. Med. Chem. (1993), 36(6), 733-46
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
GI



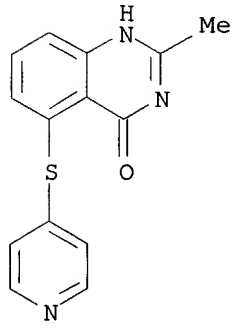
I



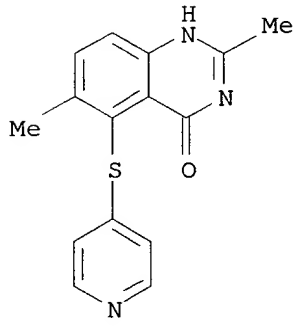
II

AB The design, synthesis, and biol. evaluation of a new class of inhibitors of thymidylate synthase (TS) is described. The mol. design was carried out by a repetitive crystallog. anal. of protein-ligand structures. The folate cofactor binding site of a high-resoln. ternary crystal complex of Escherichia coli TS, 5'-fluorodeoxyuridylate (5-FdUMP) and a classical glutamate-contg. folic acid analog was focused on. A preliminary ternary crystal structure of a novel compd. was successfully solved. Upon anal. of this initial complex, further structural elaborations were made, and a series of active 5-(arylthio)quinazolinones, e.g. I and II, was developed. The synthetic strategy was based on the displacement of a halogen at the 5-position of a quinazolinone by various aryl thioanions. The compds. were tested for inhibition of purified E. coli and/or human TS, and were assayed for cytotoxicity against three tumor cell lines in vitro. Significant thymidine protection effects were obsd. with several of the inhibitors, indicating that TS was the intracellular locus of activity.
IT **147149-61-9D**, ternary complexes with thymidylate synthase and 5-FdUMP **147149-63-1D**, ternary complexes with thymidylate synthase and 5-FdUMP

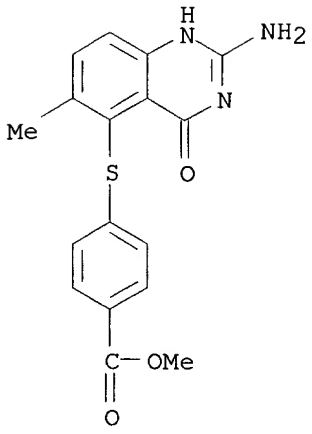
RL: PRP (Properties)
(crystal structure of)
RN 147149-61-9 CAPLUS
CN 4(1H)-Quinazolinone, 2-methyl-5-(4-pyridinylthio)- (9CI) (CA INDEX NAME)



RN 147149-63-1 CAPLUS
CN 4(1H)-Quinazolinone, 2,6-dimethyl-5-(4-pyridinylthio)- (9CI) (CA INDEX NAME)

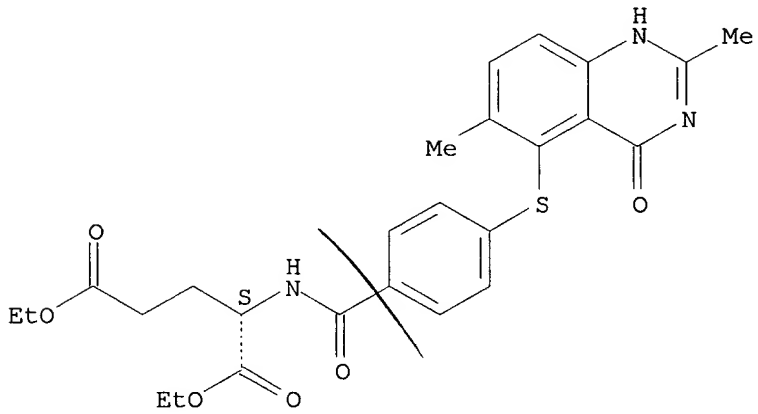


IT **147150-00-3P 147150-02-5P 147150-03-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrolysis of)
RN 147150-00-3 CAPLUS
CN Benzoic acid, 4-[(2-amino-1,4-dihydro-6-methyl-4-oxo-5-quinazolinyl)thio]-, methyl ester (9CI) (CA INDEX NAME)



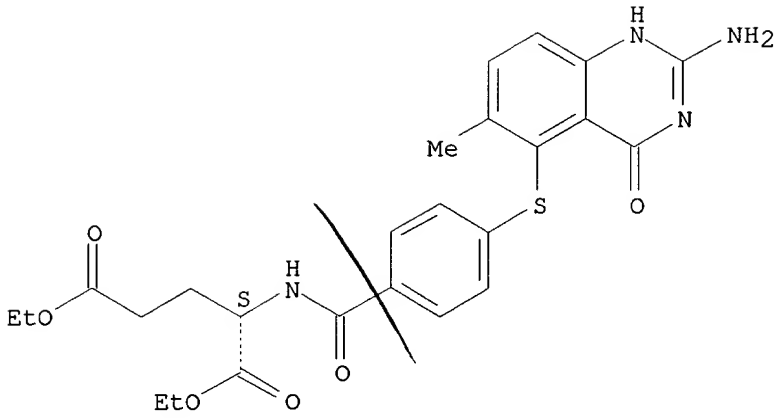
RN 147150-02-5 CAPLUS
CN L-Glutamic acid, N-[4-[(1,4-dihydro-2,6-dimethyl-4-oxo-5-quinazolinyl)thio]benzoyl]-, diethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

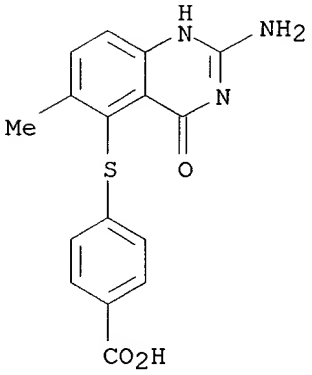


RN 147150-03-6 CAPLUS
CN L-Glutamic acid, N-[4-[(2-amino-1,4-dihydro-6-methyl-4-oxo-5-quinazolinyl)thio]benzoyl]-, diethyl ester (9CI) (CA INDEX NAME)

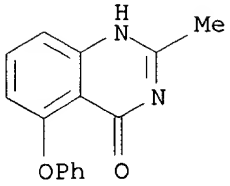
Absolute stereochemistry.



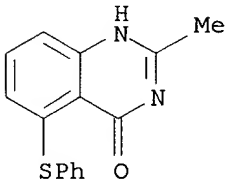
IT **147150-01-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with glutamic acid di-Et ester hydrochloride)
RN 147150-01-4 CAPLUS
CN Benzoic acid, 4-[(2-amino-1,4-dihydro-6-methyl-4-oxo-5-quinazolinyl)thio]- (9CI) (CA INDEX NAME)



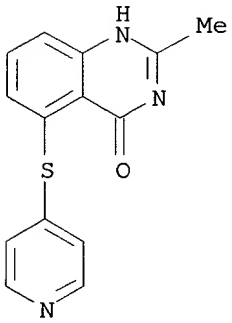
IT **147149-59-5P 147149-60-8P 147149-61-9P**
147149-62-0P 147149-63-1P 147149-64-2P
147149-65-3P 147149-66-4P 147149-67-5P
147149-68-6P 147149-69-7P 147149-70-0P
147149-71-1P 147149-72-2P 147149-73-3P
147149-74-4P 147149-75-5P 147149-76-6P
147149-77-7P 147149-78-8P 147149-79-9P
147149-80-2P 147149-81-3P 147149-82-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and thymidylate synthase inhibitor activity of)
RN 147149-59-5 CAPLUS
CN 4(1H)-Quinazolinone, 2-methyl-5-phenoxy- (9CI) (CA INDEX NAME)



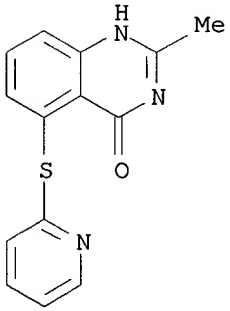
RN 147149-60-8 CAPLUS
CN 4(1H)-Quinazolinone, 2-methyl-5-(phenylthio)- (9CI) (CA INDEX NAME)



RN 147149-61-9 CAPLUS
CN 4(1H)-Quinazolinone, 2-methyl-5-(4-pyridinylthio)- (9CI) (CA INDEX NAME)

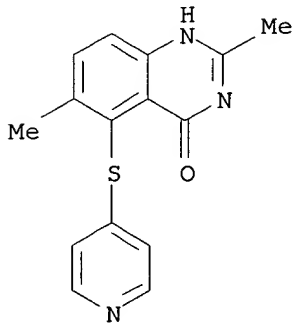


RN 147149-62-0 CAPLUS
CN 4(1H)-Quinazolinone, 2-methyl-5-(2-pyridinylthio)- (9CI) (CA INDEX NAME)

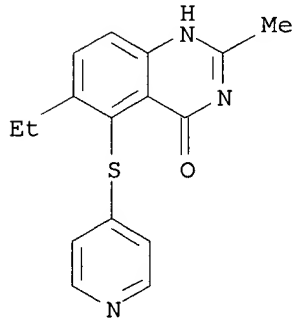


RN 147149-63-1 CAPLUS

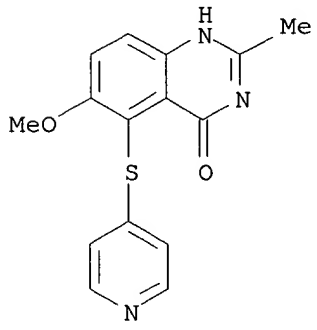
CN 4(1H)-Quinazolinone, 2,6-dimethyl-5-(4-pyridinylthio)- (9CI) (CA INDEX NAME)



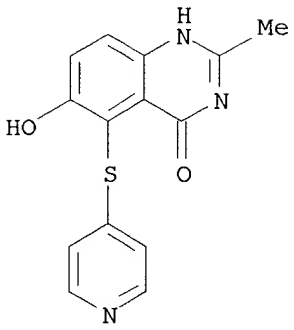
RN 147149-64-2 CAPLUS
CN 4(1H)-Quinazolinone, 6-ethyl-2-methyl-5-(4-pyridinylthio)- (9CI) (CA INDEX NAME)



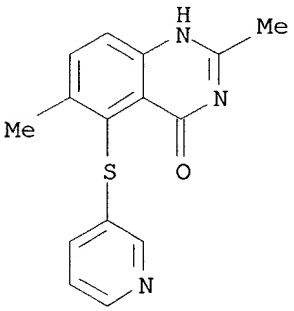
RN 147149-65-3 CAPLUS
CN 4(1H)-Quinazolinone, 6-methoxy-2-methyl-5-(4-pyridinylthio)- (9CI) (CA INDEX NAME)



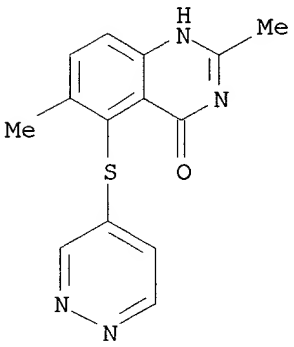
RN 147149-66-4 CAPLUS
CN 4(1H)-Quinazolinone, 6-hydroxy-2-methyl-5-(4-pyridinylthio)- (9CI) (CA INDEX NAME)



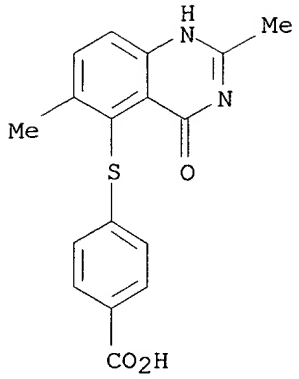
RN 147149-67-5 CAPLUS
CN 4(1H)-Quinazolinone, 2,6-dimethyl-5-(3-pyridinylthio)- (9CI) (CA INDEX NAME)



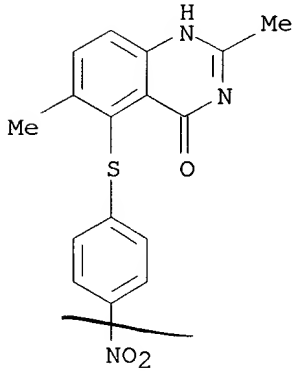
RN 147149-68-6 CAPLUS
CN 4(1H)-Quinazolinone, 2,6-dimethyl-5-(4-pyridazinylthio)- (9CI) (CA INDEX NAME)



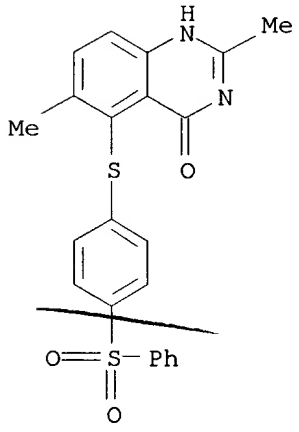
RN 147149-69-7 CAPLUS
CN Benzoic acid, 4-[(1,4-dihydro-2,6-dimethyl-4-oxo-5-quinazolinyl)thio]- (9CI) (CA INDEX NAME)



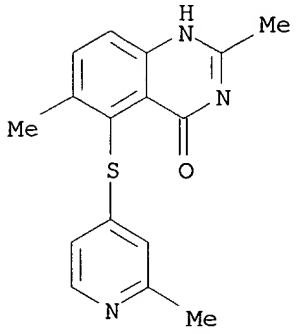
RN 147149-70-0 CAPLUS
CN 4(1H)-Quinazolinone, 2,6-dimethyl-5-[(4-nitrophenyl)thio]- (9CI) (CA INDEX NAME)



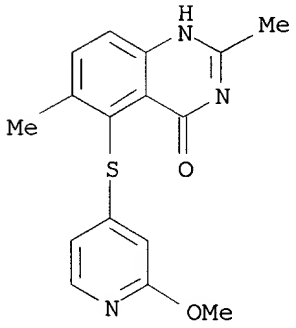
RN 147149-71-1 CAPLUS
CN 4(1H)-Quinazolinone, 2,6-dimethyl-5-[[4-(phenylsulfonyl)phenyl]thio]- (9CI) (CA INDEX NAME)



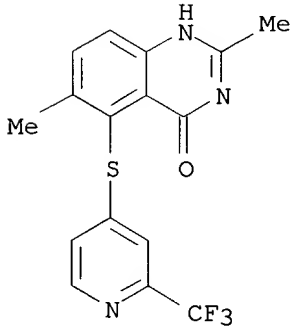
RN 147149-72-2 CAPLUS
CN 4(1H)-Quinazolinone, 2,6-dimethyl-5-[(2-methyl-4-pyridinyl)thio]- (9CI) (CA INDEX NAME)



RN 147149-73-3 CAPLUS
CN 4(1H)-Quinazolinone, 5-[(2-methoxy-4-pyridinyl)thio]-2,6-dimethyl- (9CI) (CA INDEX NAME)

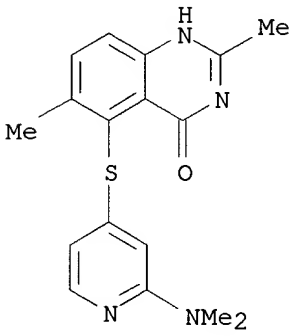


RN 147149-74-4 CAPLUS
CN 4(1H)-Quinazolinone, 2,6-dimethyl-5-[[2-(trifluoromethyl)-4-pyridinyl]thio]- (9CI) (CA INDEX NAME)

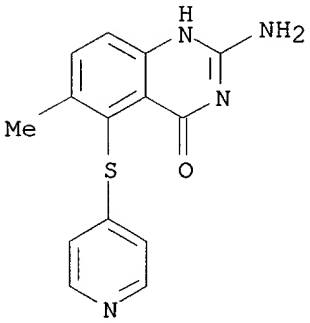


RN 147149-75-5 CAPLUS

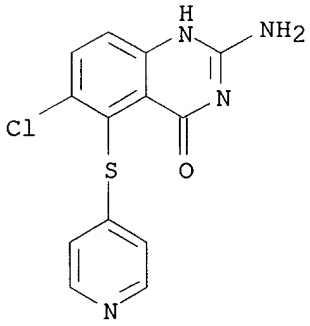
CN 4(1H)-Quinazolinone, 5-[[2-(dimethylamino)-4-pyridinyl]thio]-2,6-dimethyl- (9CI) (CA INDEX NAME)



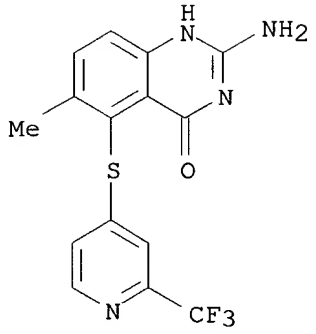
RN 147149-76-6 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridinylthio)- (9CI) (CA INDEX NAME)



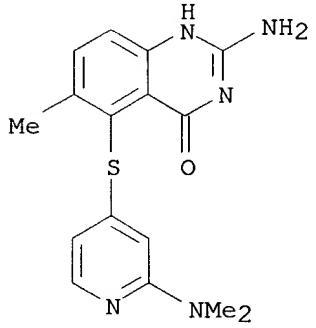
RN 147149-77-7 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-chloro-5-(4-pyridinylthio)- (9CI) (CA INDEX NAME)



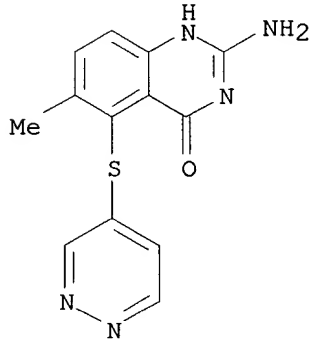
RN 147149-78-8 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-[[2-(trifluoromethyl)-4-pyridinyl]thio]- (9CI) (CA INDEX NAME)



RN 147149-79-9 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-5-[[2-(dimethylamino)-4-pyridinyl]thio]-6-methyl- (9CI) (CA INDEX NAME)

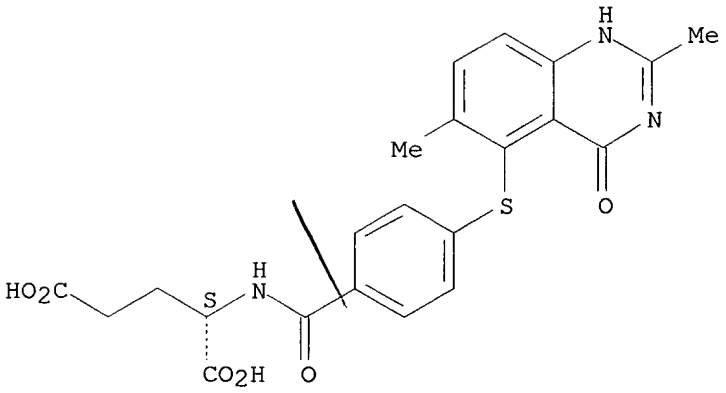


RN 147149-80-2 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-6-methyl-5-(4-pyridazinylthio)- (9CI) (CA INDEX NAME)



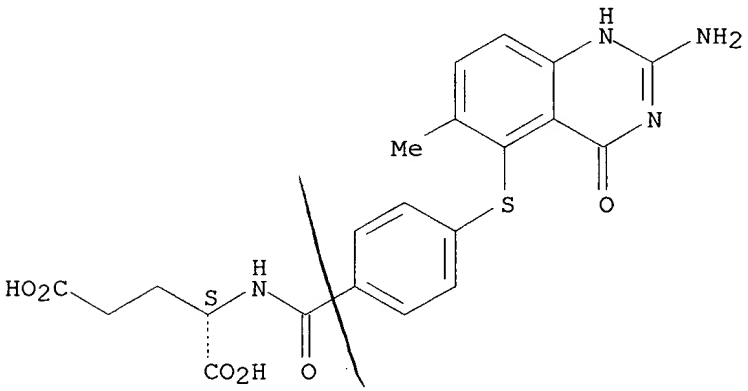
RN 147149-81-3 CAPLUS
CN L-Glutamic acid, N-[4-[(1,4-dihydro-2,6-dimethyl-4-oxo-5-quinazolinyl)thio]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

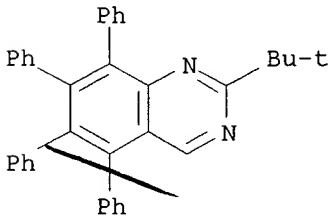


RN 147149-82-4 CAPLUS
CN L-Glutamic acid, N-[4-[(2-amino-1,4-dihydro-6-methyl-4-oxo-5-quinazolinyl)thio]benzoyl]- (9CI) (CA INDEX NAME)

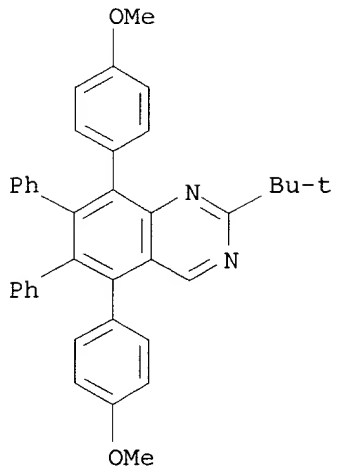
Absolute stereochemistry.



L[illegible] ANSWER 50 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1993:212203 CAPLUS
DN 118:212203
TI Reactivity of 2-tert-butyl-4,5-didehydropyrimidine and electronic structure of the parent hetaryne
AU Tielemans, Michel; Areschka, Vincent; Colomer, Jaume; Promel, Robert; Langenaeker, Wilfried; Geerlings, Paul
CS Fac. Sci., Universite Libre de Bruxelles, Brussels, B-1050, Belg.
SO Tetrahedron (1992), 48(48), 10575-86
CODEN: TETRAB; ISSN: 0040-4020
DT Journal
LA English
OS CASREACT 118:212203
AB 2-T-butyl-4,5-didehydropyrimidine, generated by oxidn. of 3-amino-5-t-butyl-3H-v-triazolo[4,5-d]pyrimidine, was allowed to react with a variety of reagents. Trapping expts. with furan and two tetracyclones gave the expected adducts in low to moderate yields. On treatment with anthracene and 1,3-cyclohexadiene, complex mixts. were obtained from which the adducts could not be isolated. Cycloaddn. of Ph azide to the intermediate yielded 3-phenyl-5-t-butyl-3H-v-triazolo[4,5-d]pyrimidine as the major product together with the unexpected 2-t-butyl-9H-pyrimido[4,5-b]indole in lesser amt. The structure of these two compds. was established by comparison with authentic specimens whose synthesis is described. Cycloaddn. also occurred with 2,3,5-tri-O-benzoyl-.beta.-D-ribofuranosyl azide to give an 8-azanucleoside in low yield. Oxidn. of the precursor in ethanol gave solely 4-ethoxy-2-t-butylpyrimidine. Oxidn. in the presence of iodine, in dichloromethane or benzene, afforded products arising from attack on the solvent, i.e. 4-chloro-5-iodo-2-t-butylpyrimidine and 5-iodo-4-phenyl-2-t-butylpyrimidine resp. In addn., 5-iodo-2-t-butyl-4(3H)-pyrimidinone was obtained in both cases. Mechanisms for these reactions are proposed. The electronic structure of 4,5-didehydropyrimidine has been calcd. by an ab initio 3-21G quantum chem. method. Both the Mol. Electrostatic Potential and the Fukui function give a very reasonable account of the strong orientation effects obsd. in the addns. to 2-t-butyl-4,5-didehydropyrimidine.
IT **118089-36-4P 118089-37-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 118089-36-4 CAPLUS
CN Quinazoline, 2-(1,1-dimethylethyl)-5,6,7,8-tetraphenyl- (9CI) (CA INDEX NAME)



RN 118089-37-5 CAPLUS
CN Quinazoline, 2-(1,1-dimethylethyl)-5,8-bis(4-methoxyphenyl)-6,7-diphenyl- (9CI) (CA INDEX NAME)


OMe
Ph
N
Bu-t
N
Ph
OMe

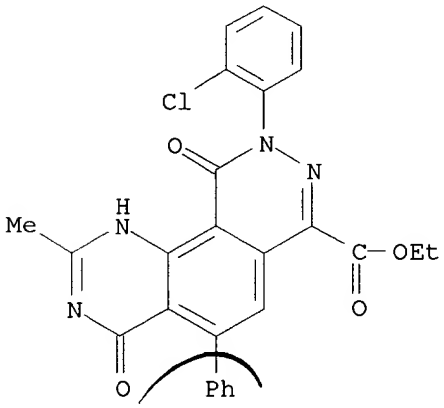
L14 ANSWER 51 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1992:235556 CAPLUS
DN 116:235556
TI Synthesis of new polyfunctionally substituted pyridazines, pyridopyridazines, thienopyridazines and phthalazines
AU Harb, Abdel Fattah Ali
CS Fac. Sci., Assiut Univ., Assiut, Egypt
SO Bull. Fac. Sci., Assiut Univ. (1991), 20(2), 65-76
CODEN: BSAUDW; ISSN: 0366-4740
DT Journal
LA English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

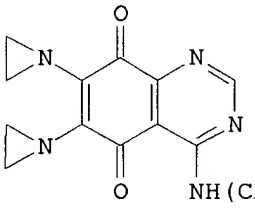
AB Title compds., including, I (R = NHNH2, R1 = Me), II, III, and IV, were prepd. from 2-ClC6H4NHN:C(CO2Et)COMe and NCCH2CO2Et via the key intermediate I (R = EtO, R1 = Me). Thus, I (R = EtO, R1 = Me) condensed with PhCHO in the presence of piperidine in EtOH to give I (R = EtO, R1 = CH:CHPh), which underwent ammonolysis to give I (R = NH2, R1 = CH:CHPh). Heating the latter compd. at 230-240.degree. gave pyridopyridazinedione II.

IT **141277-06-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 141277-06-7 CAPLUS
CN Pyridazino[4,5-h]quinazoline-7-carboxylic acid, 9-(2-chlorophenyl)-1,4,9,10-tetrahydro-2-methyl-4,10-dioxo-5-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 52 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1991:42715 CAPLUS
DN 114:42715
TI Heterocyclic quinones. XVII. A new in vivo active antineoplastic drug: 6,7-bis(1-aziridinyl)-4-[[3-(N,N-dimethylamino)propyl]amino]-5,8-quinazolinedione
AU Giorgi-Renault, Sylviane; Renault, Jean; Gebel-Servolles, Patricia; Baron, Michel; Paoletti, Claude; Cros, Suzanne; Bissery, Marie Christine; Lavelle, Francois; Atassi, Ghanem
CS Fac. Sci. Pharm. Biol., Univ. Rene Descartes, Paris, 75270, Fr.
SO J. Med. Chem. (1991), 34(1), 38-46
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
OS CASREACT 114:42715
GI

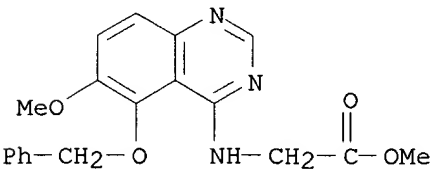


II

AB A series of heterocyclic quinones, 6-substituted and 6,7-disubstituted 4-(alkylamino)-5,8-quinazolinediones, e.g., I (R = Me, Et; n = 2,3), have been synthesis in order to evaluate their in vitro cytotoxicity on L1210 leukemia cells. Among 14 derivs. studied for the structure-activity relationship, the most potent cytotoxic compd. was aziridinylquinazolinedione II. II was tested with the use of a cell-image processor on human mammary and human melanoma cell lines. The results show that II influences cell proliferation and blocks both cells lines in the S phase. In vivo antineopolastic activity was demonstrated on a broad spectrum of murine exptl. models, but was found highly toxic and produced long-delayed deaths.

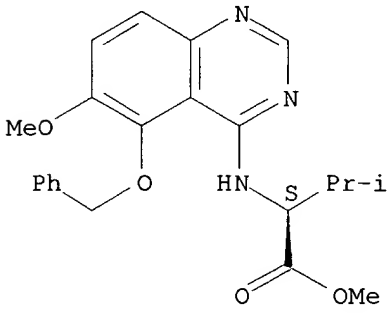
IT **120075-61-8P 120075-62-9P 120075-63-0P**
120075-64-1P 120075-65-2P 120075-66-3P
120075-67-4P 120075-68-5P 120075-69-6P
120075-70-9P 130436-81-6P 130436-82-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and debenzylation of)

RN 120075-61-8 CAPLUS
CN Glycine, N-[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]-, methyl ester (9CI) (CA INDEX NAME)



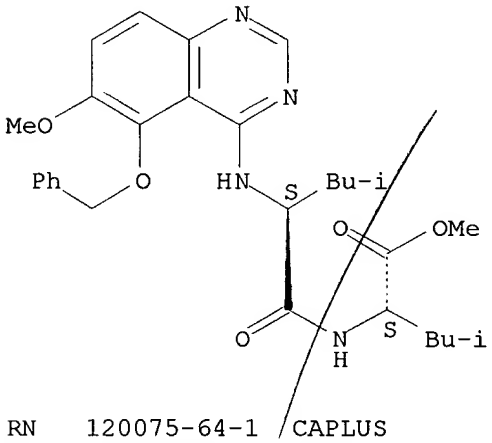
RN 120075-62-9 CAPLUS
CN L-Valine, N-[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

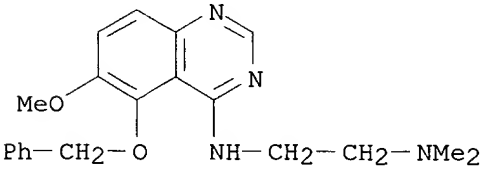


RN 120075-63-0 CAPLUS
CN L-Leucine, N-[N-[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]-L-leucyl]-, methyl ester (9CI) (CA INDEX NAME)

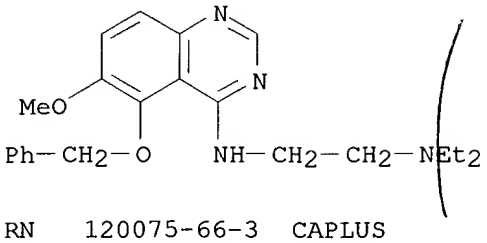
Absolute stereochemistry.



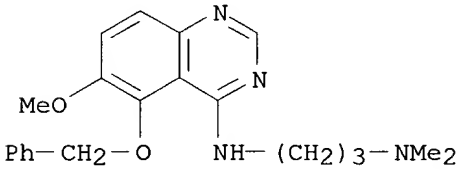
RN 120075-64-1 CAPLUS
CN 1,2-Ethanediamine, N'-[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)



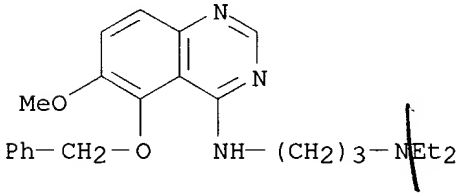
RN 120075-65-2 CAPLUS
CN 1,2-Ethanediamine, N,N-diethyl-N'-[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]- (9CI) (CA INDEX NAME)



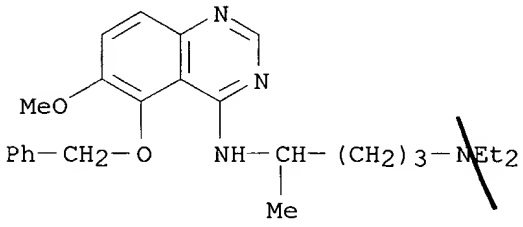
RN 120075-66-3 CAPLUS
CN 1,3-Propanediamine, N'-[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)



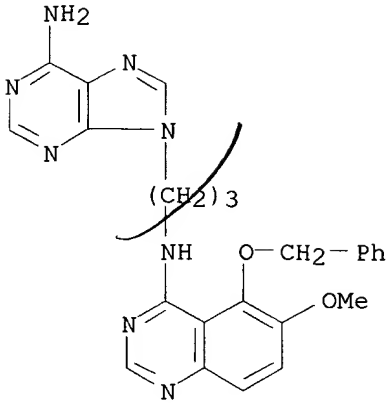
RN 120075-67-4 CAPLUS
CN 1,3-Propanediamine, N,N-diethyl-N'-[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]- (9CI) (CA INDEX NAME)



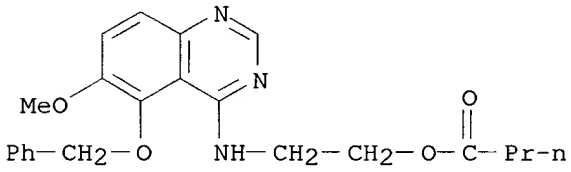
RN 120075-68-5 CAPLUS
CN 1,4-Pentanediamine, N1,N1-diethyl-N4-[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]- (9CI) (CA INDEX NAME)



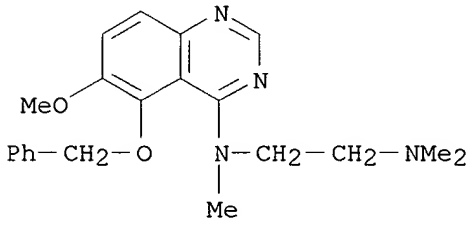
RN 120075-69-6 CAPLUS
CN 4-Quinazolinamine, N-[3-(6-amino-9H-purin-9-yl)propyl]-6-methoxy-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



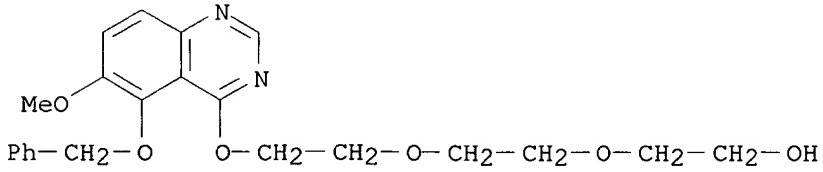
RN 120075-70-9 CAPLUS
CN Butanoic acid, 2-[[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]amino]ethyl ester (9CI) (CA INDEX NAME)



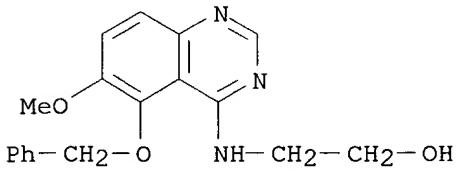
RN 130436-81-6 CAPLUS
CN 1,2-Ethanediamine, N-[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]-N,N',N'-trimethyl- (9CI) (CA INDEX NAME)



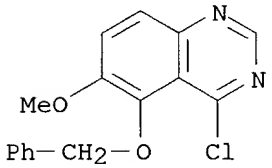
RN 130436-82-7 CAPLUS
CN Ethanol, 2-[2-[2-[[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]oxy]ethoxy]ethoxy]- (9CI) (CA INDEX NAME)



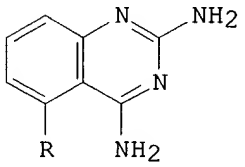
IT **120075-60-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn., acylation, and debenzylation of)
RN 120075-60-7 CAPLUS
CN Ethanol, 2-[[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)



IT **120075-53-8**
RL: RCT (Reactant)
(substitution reactions of, with amines and triethylene glycol)
RN 120075-53-8 CAPLUS
CN Quinazoline, 4-chloro-6-methoxy-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



L14 ANSWER 53 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1990:55769 CAPLUS
DN 112:55769
TI Antifolate and antibacterial activities of 5-substituted 2,4-diaminoquinazolines
AU Harris, Neil V.; Smith, Christopher; Bowden, Keith
CS Dagenham Res. Cent., Rhone-Poulenc Ltd., Dagenham/Essex, RM10 7XS, UK
SO J. Med. Chem. (1990), 33(1), 434-44
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
OS CASREACT 112:55769
GI

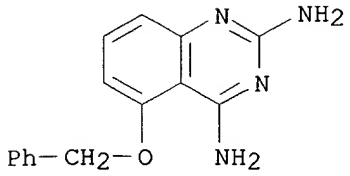


I

AB A series of 5-substituted 2,4-diaminoquinazolines I (R = alkoxy, alkylthio, dialkylamino) has been synthesized starting from 2,6-dinitrobenzonitrile by substitution, redn., followed by cyclization with chloroformamidine hydrochloride, and evaluated as inhibitors of the enzyme dihydrofolate reductase (DHFR) from both bacterial and mammalian sources. The best compds., e.g. I (R = OMe), show good activity against E. coli DHFR, but there is no significant selectivity for the bacterial over the mammalian enzyme. The structure-activity relationships for enzyme inhibition appear to be complex and not amenable to simple anal.; a hypothesis to explain the obsd. qual. structure-activity relationships is proposed. The inhibitory activities of the compds. against the growth of intact bacterial cells in vitro closely parallel those for the inhibition of the isolated bacterial enzymes, suggesting that their antifolate action is responsible for their antibacterial effects. Five of the compds. were tested for their ability to cure a systemic E. coli infection in the mouse, but they showed no therapeutic effects at their max. tolerated doses.

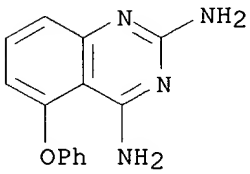
IT **123241-62-3P** **123241-63-4P** **123241-67-8P**
123241-74-7P **123241-79-2P** **123241-95-2P**
123241-96-3P **123241-99-6P** **123242-02-4P**
123242-05-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., antibacterial, and dihydrofolate reductase inhibition activity of)

RN 123241-62-3 CAPLUS
CN 2,4-Quinazolinediamine, 5-(phenylmethoxy)-, monohydrochloride (9CI) (CA INDEX NAME)



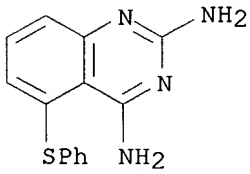
● HCl

RN 123241-63-4 CAPLUS
CN 2,4-Quinazolinediamine, 5-phenoxy-, monohydrochloride (9CI) (CA INDEX NAME)



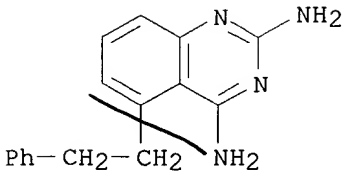
● HCl

RN 123241-67-8 CAPLUS
CN 2,4-Quinazolinediamine, 5-(phenylthio)-, monohydrochloride (9CI) (CA INDEX NAME)



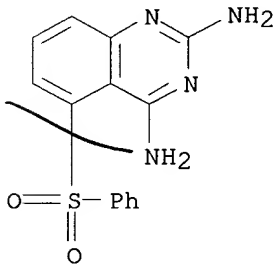
● HCl

RN 123241-74-7 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-phenylethyl)-, monohydrochloride (9CI) (CA INDEX NAME)



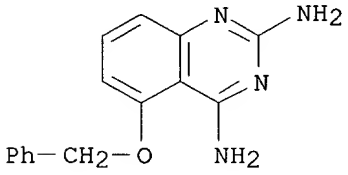
● HCl

RN 123241-79-2 CAPLUS
CN 2,4-Quinazolinediamine, 5-(phenylsulfonyl)-, monohydrochloride (9CI) (CA INDEX NAME)

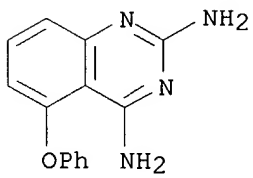


● HCl

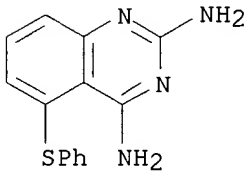
RN 123241-95-2 CAPLUS
CN 2,4-Quinazolinediamine, 5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



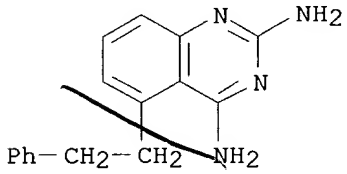
RN 123241-96-3 CAPLUS
CN 2,4-Quinazolinediamine, 5-phenoxy- (9CI) (CA INDEX NAME)



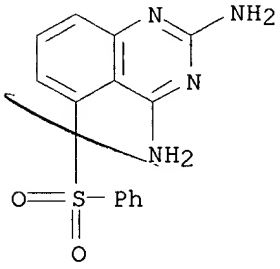
RN 123241-99-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-(phenylthio)- (9CI) (CA INDEX NAME)



RN 123242-02-4 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-phenylethyl)- (9CI) (CA INDEX NAME)

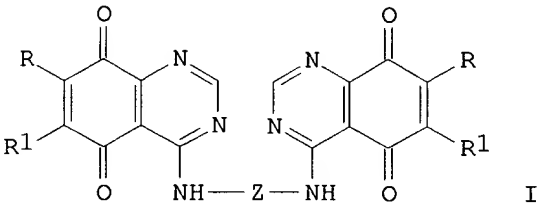


RN 123242-05-7 CAPLUS
CN 2,4-Quinazolinediamine, 5-(phenylsulfonyl)- (9CI) (CA INDEX NAME)



see 55 of 71

L1 ANSWER 54 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1989:212749 CAPLUS
DN 110:212749
TI Heterocyclic quinones. XIII. Dimerization in the series of 5,8-quinazolinediones: synthesis and antitumor effects of bis(4-amino-5,8-quinazolinediones)
AU Giorgi-Renault, Sylviane; Renault, Jean; Baron, Michel; Gebel-Servolles, Patricia; Delic, Jozo; Cros, Suzanne; Paoletti, Claude
CS Fac. Sci. Pharm. Biol., Univ. Rene Descartes, Paris, 75270, Fr.
SO Chem. Pharm. Bull. (1988), 36(10), 3933-47
CODEN: CPBTAL; ISSN: 0009-2363
DT Journal
LA English
OS CASREACT 110:212749
GI

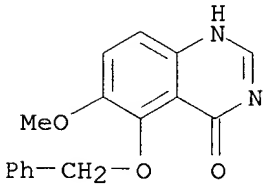


I

AB A series of dimers, e.g., I [R = H, R1 = OMe; R = R1 = 1-aziridinyl; Z = CH2CH2, (CH2)7, (CH2)3NMe(CH2)3, CH2(CH2OCH2)2CH2], of 5,8-quinazolinediones linked in the 4-position by a simple or a substituted .alpha.,.omega.-diaminopolymethylene chain was studied. The structure-activity relationships of I are discussed as functions of the chain length, presence or absence of other functional groups, nature of these groups, position of the chain, and nature of R and R1. I (R = OMe) showed variable cytotoxicity toward L1210 leukemia cells. I (R = R1 = 1-aziridinyl) which exhibited high cytotoxic activity (IC50 = 0.0037 to 0.018 .mu.M) were further screened in vivo for activity against murine P388 leukemia. The most potent compd. was I [R = R1 = 1-aziridinyl; Z = (CH2)3NMe(CH2)3].

IT **120075-51-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and chlorination of)

RN 120075-51-6 CAPLUS
CN 4(1H)-Quinazolinone, 6-methoxy-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)

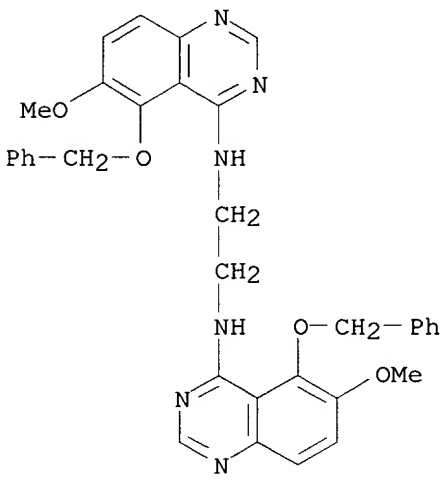


IT **120075-71-0P 120075-72-1P 120075-73-2P**
120075-74-3P 120075-75-4P 120075-76-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. and debenzylation of)

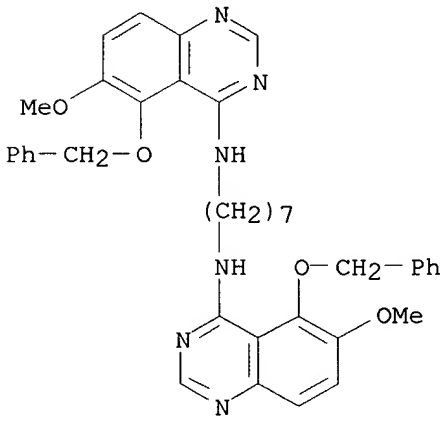
RN 120075-71-0 CAPLUS

CN 1,2-Ethanediamine, N,N'-bis[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]- (9CI) (CA INDEX NAME)



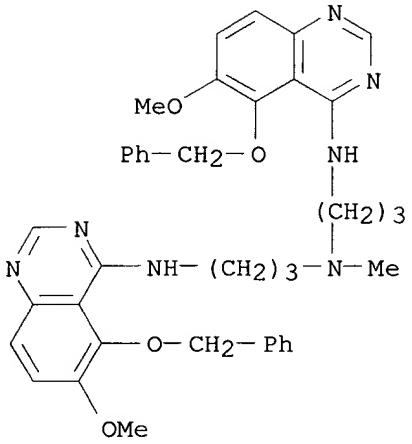
RN 120075-72-1 CAPLUS

CN 1,7-Heptanediamine, N,N'-bis[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]- (9CI) (CA INDEX NAME)



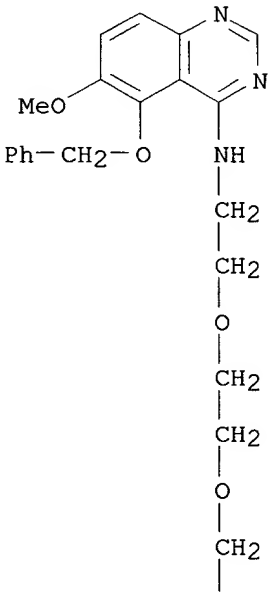
RN 120075-73-2 CAPLUS

CN 1,3-Propanediamine, N'-[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]-N-[3-[[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]amino]propyl]-N-methyl- (9CI) (CA INDEX NAME)

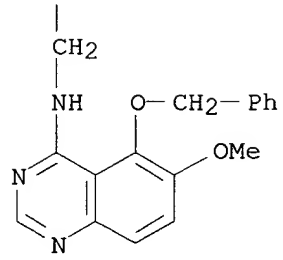


RN 120075-74-3 CAPLUS
CN 4-Quinazolinamine, N,N'-[1,2-ethanediylbis(oxy-2,1-ethanediyl)]bis[6-methoxy-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)

PAGE 1-A

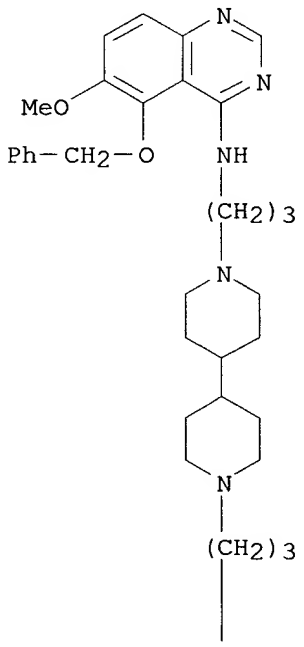


PAGE 2-A

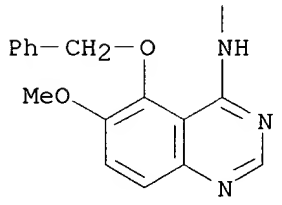


RN 120075-75-4 CAPLUS
CN [4,4'-Bipiperidine]-1,1'-dipropanamine, N,N'-bis[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

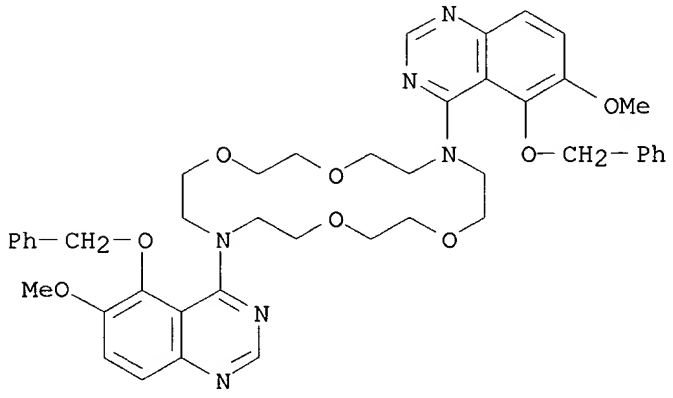


PAGE 2-A

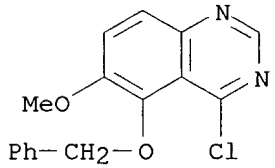


RN 120075-76-5 CAPLUS

CN Quinazoline, 4,4'-(1,4,10,13-tetraoxa-7,16-diazacyclooctadecane-7,16-diyl)bis[6-methoxy-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



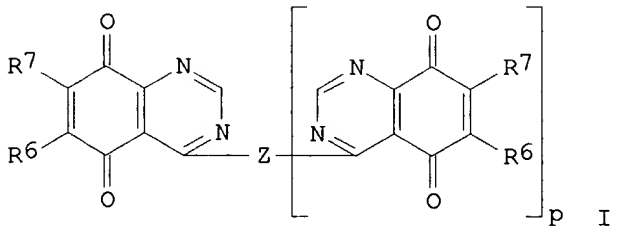
IT **120075-53-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and substitution reactions of, with diamines)
RN 120075-53-8 CAPLUS
CN Quinazoline, 4-chloro-6-methoxy-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



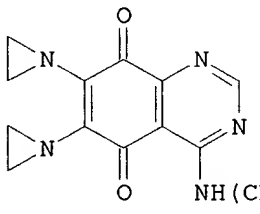
L14 ANSWER 55 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1989:173249 CAPLUS
DN 110:173249
TI 4-Amino-5,8-quinazolinedione derivatives with antitumor activity, processes and intermediates for their preparation, and pharmaceutical compositions containing them
IN Renault, Jean Armand Paul; Giorgi, Sylvianne Madeleine Jeanne; Gebel, Patricia Nadine Jeanne; Baron, Michel Jean Pierre; Paoletti, Claude Antoine; Cros, Suzanne Blanche Georgette
PA Centre National de la Recherche Scientifique, Fr.; Universite Rene Descartes
SO Eur. Pat. Appl., 146 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 292365	A2	19881123	EP 1988-401158	19880511
EP 292365	A3	19890329		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2615189	A1	19881118	FR 1987-6795	19870514
FR 2615189	B1	19890728		
WO 8808841	A1	19881117	WO 1988-FR235	19880511
W: JP, US				
PRAI FR 1987-6795		19870514		

OS CASREACT 110:173249; MARPAT 110:173249
GI



I



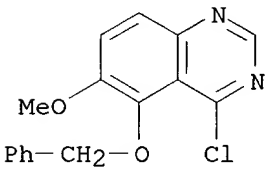
II

AB The title compds. [I; p = 0, 1; R7 = H and R6 = primary, secondary, or tertiary amino, piperidinyl, pyrrolidinyl, cyclic diamino; or R6 = R7 = 1-aziridinyl (un)substituted by 1-4 alkyls; when p = 0, Z = substituted monoalkylamino (esp. aminoalkylamino), di- to pentapeptide residue; when p = 1, Z = NHY1NH, N(Y2Y3)N; Y1 = various bridging chains; Y2, Y3 = polyoxyethyl bridges] are prepd. as antitumor agents. Oxidn. of 2-benzyloxy-3-methoxy-6-nitrobenzaldehyde with KMnO4 in Me2CO gave 71% of the benzoic acid, followed by redn. of the nitro group with FeSO4 in aq.

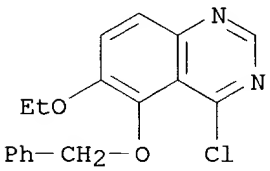
NH3 (79%), cyclization with s-triazine in EtOH contg. piperidine to give a 3,4-dihydro-4-quinazolinone (80%), and treatment of the latter with POCl3 and Et3N in C6H6 to give 80% 5-benzyloxy-4-chloro-6-methoxyquinazoline. Aminolysis with H2N(CH2)3NMe2 gave 95% 4-amino deriv., which underwent debenzylation by hydrogenolysis or CF3CO2H treatment (80-100%), oxidn. by K nitrosodisulfonate to the quinone (48%), and reaction with excess aziridine at 0.degree. to give diaziridinyl[(dimethylamino)propylamino]quinazolinedione II. At 0.4 mg/kg/day (i.p.) for 9 days in mice inoculated i.p. with 106 P388 leukemia cells, II increased survival time to 222% of control.

IT **120075-53-8P**, 5-Benzyloxy-4-chloro-6-methoxyquinazoline
120075-54-9P, 5-Benzyloxy-4-chloro-6-ethoxyquinazoline
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and aminolysis of)

RN 120075-53-8 CAPLUS
CN Quinazoline, 4-chloro-6-methoxy-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)

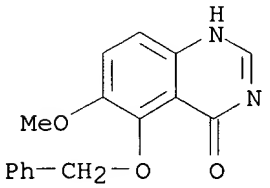


RN 120075-54-9 CAPLUS
CN Quinazoline, 4-chloro-6-ethoxy-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)

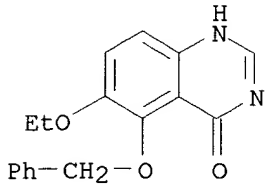


IT **120075-51-6P**, 5-Benzyloxy-6-methoxy-3,4-dihydro-4-quinazolinone
120075-52-7P, 5-Benzyloxy-6-ethoxy-3,4-dihydro-4-quinazolinone
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and conversion of, to chloroquinazoline deriv.)

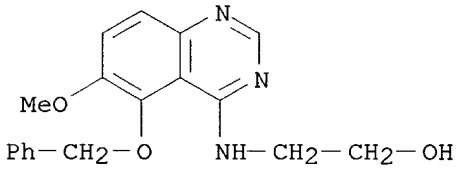
RN 120075-51-6 CAPLUS
CN 4(1H)-Quinazolinone, 6-methoxy-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



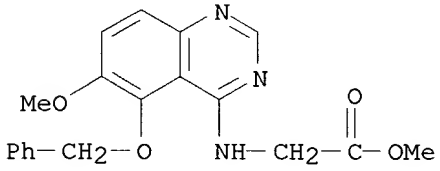
RN 120075-52-7 CAPLUS
CN 4(1H)-Quinazolinone, 6-ethoxy-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



IT **120075-60-7P 120075-61-8P 120075-62-9P**
120075-63-0P 120075-64-1P 120075-65-2P
120075-66-3P 120075-67-4P 120075-68-5P
120075-69-6P 120075-70-9P 120075-71-0P
120075-72-1P 120075-73-2P 120075-74-3P
120075-75-4P 120075-76-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and debenzylation-oxidn. of)
RN 120075-60-7 CAPLUS
CN Ethanol, 2-[[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

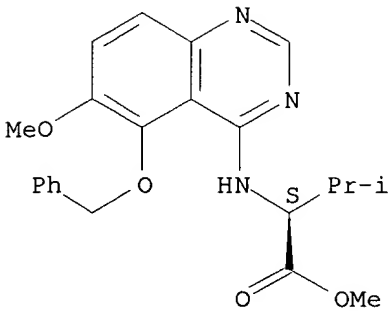


RN 120075-61-8 CAPLUS
CN Glycine, N-[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]-, methyl ester (9CI) (CA INDEX NAME)



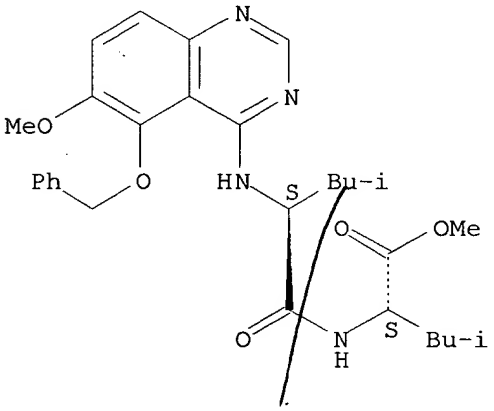
RN 120075-62-9 CAPLUS
CN L-Valine, N-[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

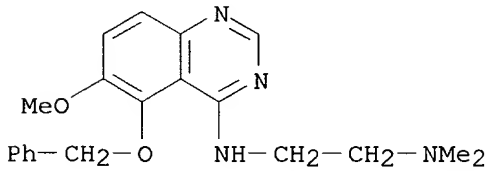


RN 120075-63-0 CAPLUS
CN L-Leucine, N-[N-[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]-L-leucyl]-, methyl ester (9CI) (CA INDEX NAME)

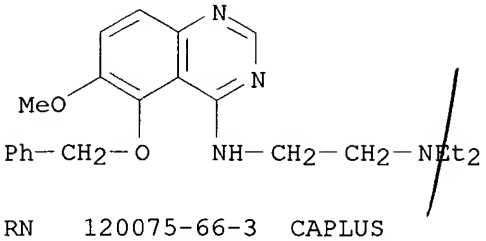
Absolute stereochemistry.



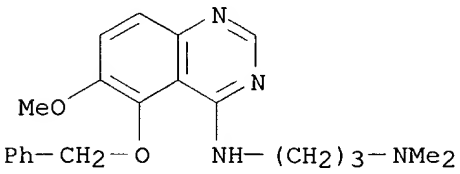
RN 120075-64-1 CAPLUS
CN 1,2-Ethanediamine, N'-[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)



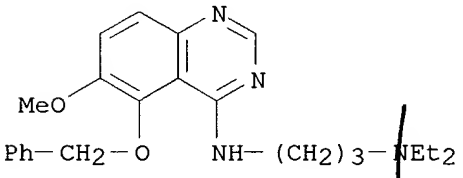
RN 120075-65-2 CAPLUS
CN 1,2-Ethanediamine, N,N-diethyl-N'-[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]- (9CI) (CA INDEX NAME)



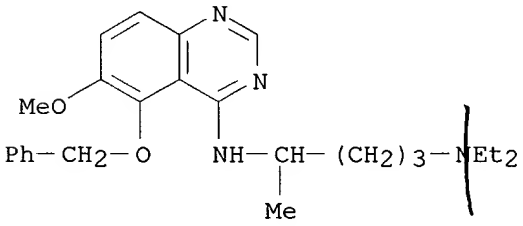
RN 120075-66-3 CAPLUS
CN 1,3-Propanediamine, N'-[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)



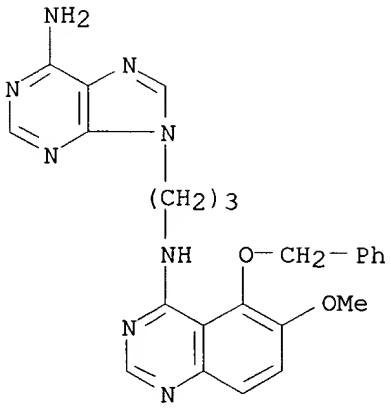
RN 120075-67-4 CAPLUS
CN 1,3-Propanediamine, N,N-diethyl-N'-[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]- (9CI) (CA INDEX NAME)



RN 120075-68-5 CAPLUS
CN 1,4-Pentanediamine, N1,N1-diethyl-N4-[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]- (9CI) (CA INDEX NAME)

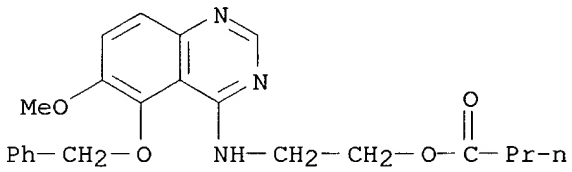


RN 120075-69-6 CAPLUS
CN 4-Quinazolinamine, N-[3-(6-amino-9H-purin-9-yl)propyl]-6-methoxy-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)

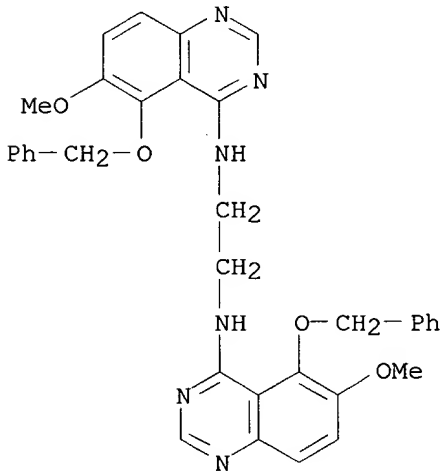


RN 120075-70-9 CAPLUS
CN Butanoic acid, 2-[[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]amino]ethyl ester (9CI) (CA INDEX NAME)

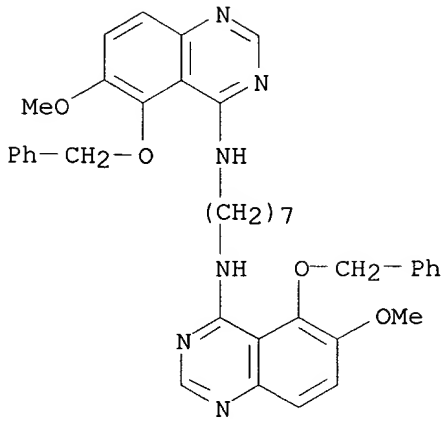
see 529 71



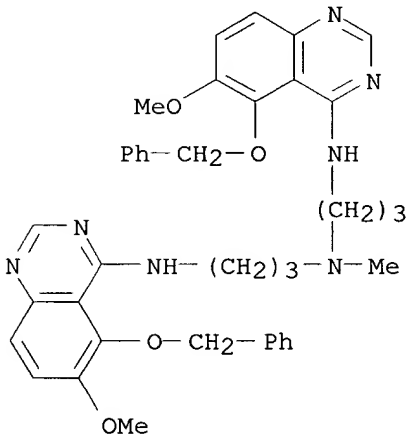
RN 120075-71-0 CAPLUS
CN 1,2-Ethanediamine, N,N'-bis[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]- (9CI) (CA INDEX NAME)



RN 120075-72-1 CAPLUS
CN 1,7-Heptanediamine, N,N'-bis[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]- (9CI) (CA INDEX NAME)

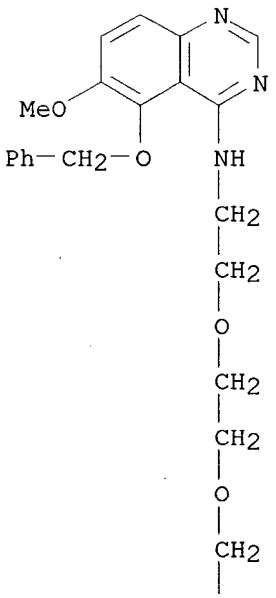


RN 120075-73-2 CAPLUS
CN 1,3-Propanediamine, N'-[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]-N-[3-[[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]amino]propyl]-N-methyl- (9CI) (CA INDEX NAME)

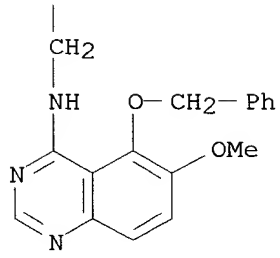


RN 120075-74-3 CAPLUS
CN 4-Quinazolinamine, N,N'-[1,2-ethanediylbis(oxy-2,1-ethanediyl)]bis[6-methoxy-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)

PAGE 1-A

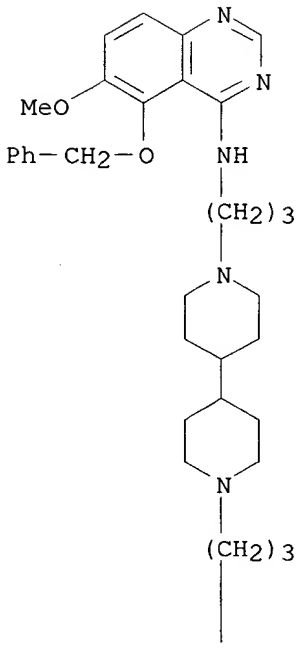


PAGE 2-A

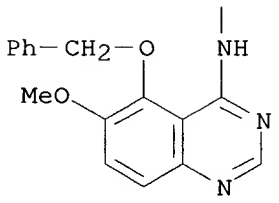


RN 120075-75-4 CAPLUS
CN [4,4'-Bipiperidine]-1,1'-dipropanamine, N,N'-bis[6-methoxy-5-(phenylmethoxy)-4-quinazolinyl]- (9CI) (CA INDEX NAME)

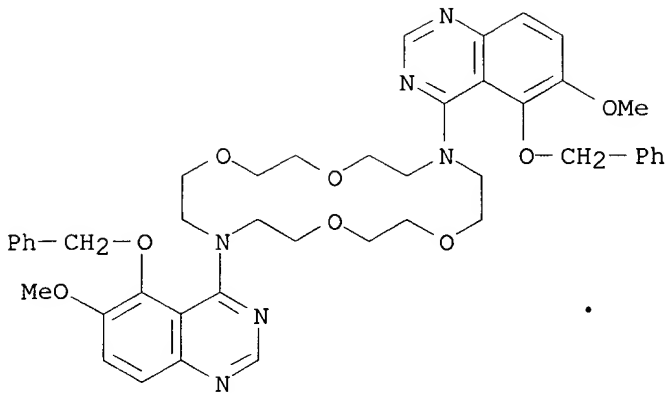
PAGE 1-A



PAGE 2-A



RN 120075-76-5 CAPLUS
CN Quinazoline, 4,4'-(1,4,10,13-tetraoxa-7,16-diazacyclooctadecane-7,16-diyl)bis[6-methoxy-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)


N
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Ph—CH2—O
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MeO
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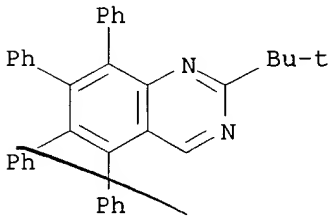
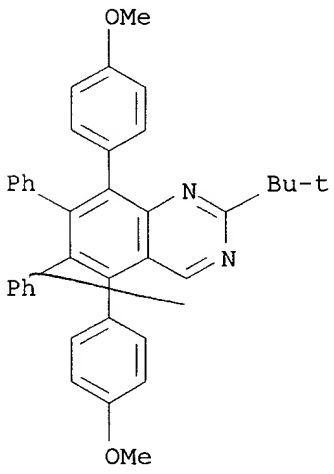
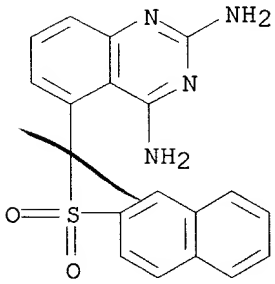
L14 ANSWER 56 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1989:74516 CAPLUS
DN 110:74516
TI Reactivity and electronic structure of a 4,5-didehydropyrimidine
AU Tielemans, Michel; Promel, Robert; Geerlings, Paul
CS Fac. Sci., Univ. Libre de Bruxelles, Brussels, B-1050, Belg.
SO Tetrahedron Lett. (1988), 29(14), 1687-90
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
OS CASREACT 110:74516
AB Reactions of 2-tert-butyl-4,5-didehydropyrimidine (I) with 1,3-dienes, 2 1,3-dipoles (azides), an electrophile (iodine) and a nucleophile (EtOH) were studied. The results are correlated with the electronic structure of 4,5-didehydropyrimidine calcd. by an ab initio quantum-chem. method.
IT **118089-36-4P 118089-37-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 118089-36-4 CAPLUS
CN Quinazoline, 2-(1,1-dimethylethyl)-5,6,7,8-tetraphenyl- (9CI) (CA INDEX NAME)



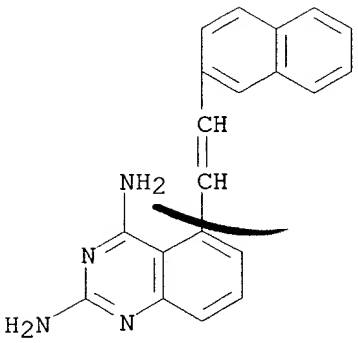
RN 118089-37-5 CAPLUS
CN Quinazoline, 2-(1,1-dimethylethyl)-5,8-bis(4-methoxyphenyl)-6,7-diphenyl- (9CI) (CA INDEX NAME)



L14 ANSWER 57 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1985:571456 CAPLUS
DN 103:171456
TI Comparative QSAR of antibacterial dihydrofolate reductase inhibitors
AU Coats, Eugene A.; Genther, Clara S.; Smith, Carl C.
CS Coll. Pharm., Univ. Cincinnati, Cincinnati, OH, USA
SO QSAR Des. Bioact. Compd. (1984), 71-85. Editor(s): Kuchar, M. Publisher: Prous, Barcelona, Spain.
CODEN: 53SIAU
DT Conference
LA English
AB The quant. structure-activity relationship (QSAR) of pteridines, pyrimidines, triazines, and quinazolines with regard to inhibition of dihydrofolate reductase (DHFR) [9002-03-3] of Lactobacillus casei was studied. The results were interpreted in light of the known x-ray crystal structure of the ternary complex of L. casei DHFR with methotrexate and NADPH and with ref. to previously conducted QSAR studies on isolated L. casei DHFR. The correlations obtained for pteridines, pyrimidines, and phenyltriazines provide a logical extension of the known methotrexate L. casei-DHFR interactions. In case of quinazolines, however, the results of QSAR do not match with the available conceptualization of inhibitor-active site interaction; the possible modes of quinazoline-DHFR interaction thus remain as conjecture or hypothesis until further exptl. data are available.
IT **50828-20-1 98747-33-2**
RL: BIOL (Biological study)
(dihydrofolate reductase inhibition by, QSAR of)
RN 50828-20-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)



RN 98747-33-2 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethenyl]- (9CI) (CA INDEX NAME)


CH
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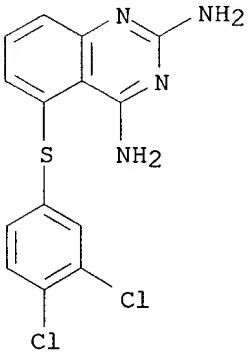
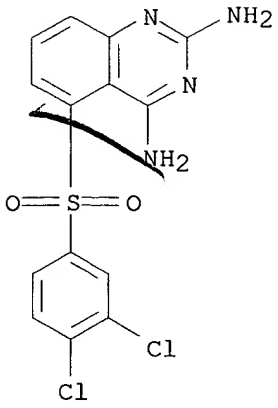
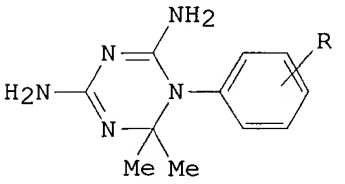
L14 ANSWER 58 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1984:416805 CAPLUS
DN 101:16805
TI A general distance-geometry three-dimensional receptor model for diverse dihydrofolate reductase inhibitors
AU Ghose, Arup K.; Crippen, Gordon M.
CS Dep. Chem., Texas A and M Univ., College Station, TX, 77943, USA
SO J. Med. Chem. (1984), 27(7), 901-14
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
AB A common 3-dimensional receptor model was formulated for 6 classes of rat liver dihydrofolate reductase [9002-03-3] inhibitors by using the distance geometry approach. Sixty-two compds. (pyridopyrimidines, pyrimidines, pyrroloquinazolines, quinazolines, and triazines) were used to generate the receptor model, which has 11 attractive site points and 5 repulsive ones. It gave a fit having a correlation coeff. of 0.949 and root mean square deviation of 0.527. The model successfully predicted the biol. data of 33 mols. of 5 different classes, one mol. of which was a member of a new class not included in the original data set. Guidelines are put forth for the synthesis of improved inhibitors.
IT **50828-12-1 50828-14-3**
RL: BIOL (Biological study)
(dihydrofolate reductase inhibitor, general distance-geometry three-dimensional receptor model for)
RN 50828-12-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)thio]- (9CI) (CA INDEX NAME)



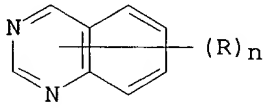
RN 50828-14-3 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)


N
NH2
N
NH2
O
S
O
Cl
Cl

L14 ANSWER 59 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1983:447537 CAPLUS
DN 99:47537
TI Combined distance geometry analysis of dihydrofolate reductase inhibition by quinazolines and triazines
AU Ghose, Arup K.; Crippen, Gordon M.
CS Dep. Chem., Texas A and M Univ., College Station, TX, 77843, USA
SO J. Med. Chem. (1983), 26(7), 996-1010
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
GI



I



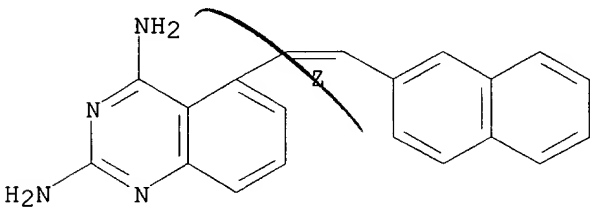
II

AB QSAR anal. of triazines I (R = H, Br, F, I, Me, MeO, CF3, PhCH2O, etc.) and quinazolines II R = H, OH, SH, H2N, AcNH, Me, etc.; n = 1-3) as inhibitors of rat liver dihydrofolate reductase [9002-03-3] using distance geometry anal. is described. The model was applied to predict the biol. activity of 91 compds. The predicted values showed a root mean square deviation of 0.907 and a correlation coeff. of 0.790. The distance geometry model for the dihydrofolate reductase inhibition is unique in its ability to fit 3 different sets of mols. (3'- and 4'-substituted phenyltriazines and quinazolines) in the same model, and successfully predicts the biol. activity of the compds.

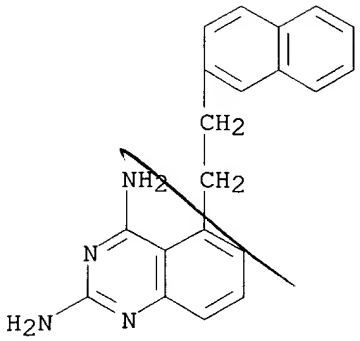
IT **50828-08-5 50828-09-6 50828-12-1**
50828-13-2 50828-14-3 50828-17-6
50828-19-8 50828-20-1 50828-21-2
50930-12-6
RL: BIOL (Biological study)
(dihydrofolate reductase inhibition by, distance geometry anal. in prediction of)

RN 50828-08-5 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethenyl]-, (Z)- (9CI) (CA INDEX NAME)

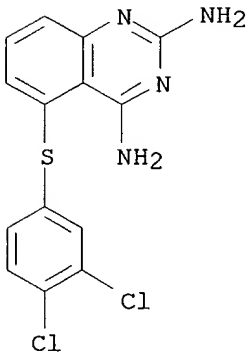
Double bond geometry as shown.



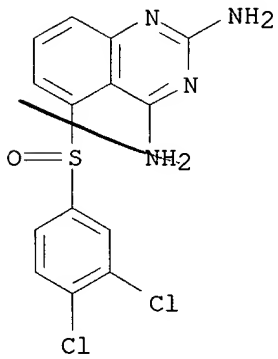
RN 50828-09-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethyl]- (9CI) (CA INDEX NAME)



RN 50828-12-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)thio]- (9CI) (CA INDEX NAME)

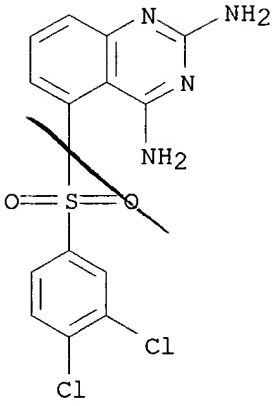


RN 50828-13-2 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)sulfinyl]- (9CI) (CA INDEX NAME)



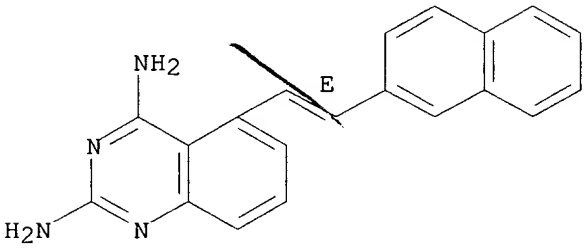
RN 50828-14-3 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX

NAME)

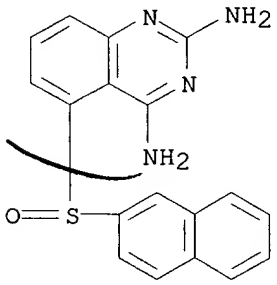


RN 50828-17-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

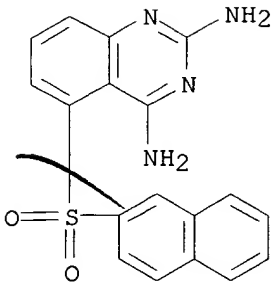
Double bond geometry as shown.



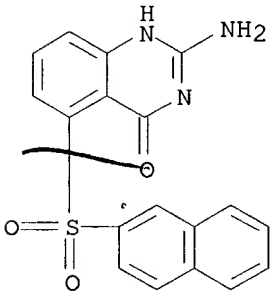
RN 50828-19-8 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylsulfinyl)- (9CI) (CA INDEX NAME)



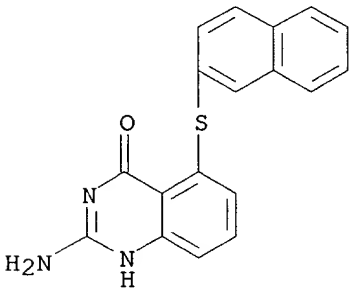
RN 50828-20-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)



RN 50828-21-2 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-5-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)

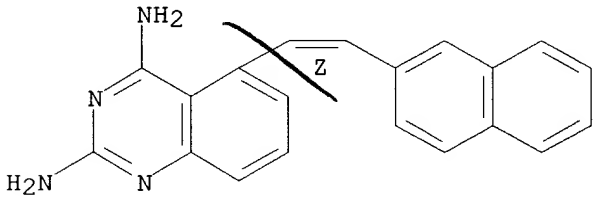


RN 50930-12-6 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-5-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

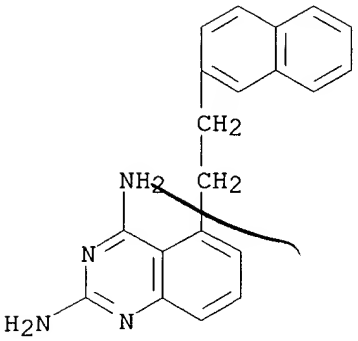


L14 ANSWER 60 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1982:451655 CAPLUS
DN 97:51655
TI Quantitative structure-activity relationship by distance geometry: quinazolines as dihydrofolate reductase inhibitors
AU Ghose, Arup K.; Crippen, Gordon M.
CS Dep. Chem., Texas A and M Univ., College Station, TX, 77843, USA
SO J. Med. Chem. (1982), 25(8), 892-9
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
AB A reinvestigation of the QSAR of 6B quinazoline inhibitors of dihydrofolate reductase is reported. As in the earlier study, the binding data fitted to an 11-point model of the site, but improved computer algorithms resulted in a much better overall fit (correlation coeff. 0.95, std. deviation 0.727 kcal) and a more accurate fit for some very loosely bound 2,4-diaminoquinazolines. Removal of 2 of the site points gave an even better fit than the original 11 site points. However, deleting a 3rd one worsened the calcd. binding energies of the loosely bound 2,4-diaminoquinazolines. The results lead to predictions of chem. modifications of the quinazolines that should improve their biol. activity.
IT **50828-08-5 50828-09-6 50828-12-1 50828-13-2 50828-14-3 50828-17-6 50828-18-7 50828-19-8 50828-20-1 50828-21-2 50930-12-6**
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); BIOL (Biological study)
(dihydrofolate reductase inhibition by, structure in relation to)
RN 50828-08-5 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethenyl]-, (Z)- (9CI) (CA INDEX NAME)

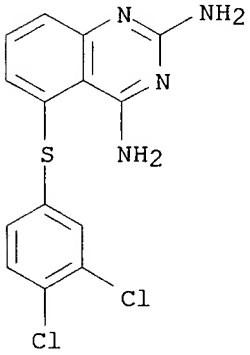
Double bond geometry as shown.



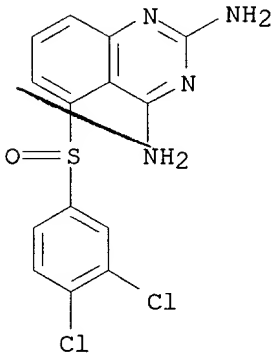
RN 50828-09-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethyl]- (9CI) (CA INDEX NAME)



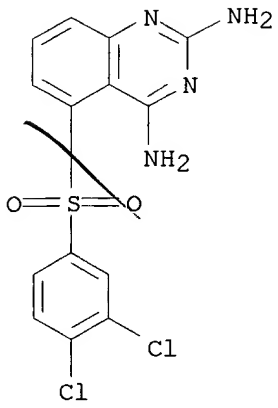
RN 50828-12-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)thio]- (9CI) (CA INDEX NAME)



RN 50828-13-2 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)sulfinyl]- (9CI) (CA INDEX NAME)

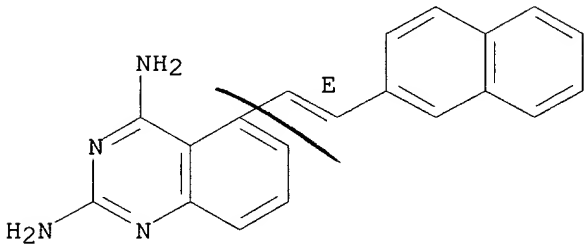


RN 50828-14-3 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

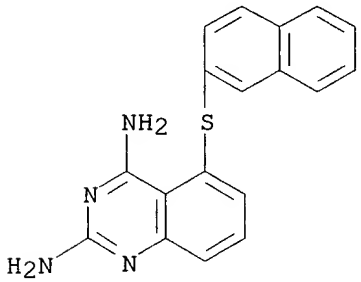


RN 50828-17-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

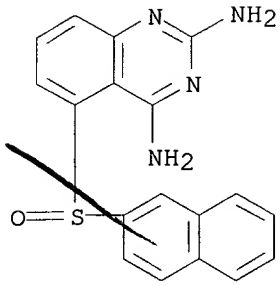
Double bond geometry as shown.



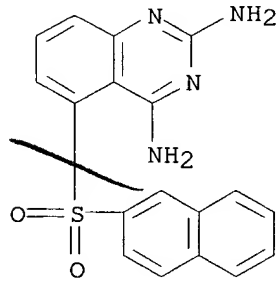
RN 50828-18-7 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)



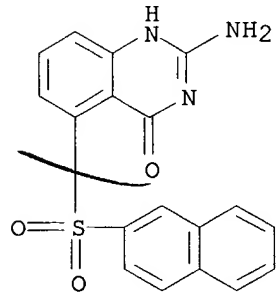
RN 50828-19-8 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylsulfinyl)- (9CI) (CA INDEX NAME)



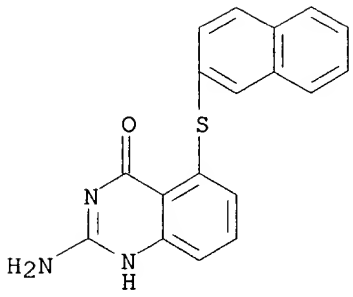
RN 50828-20-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)



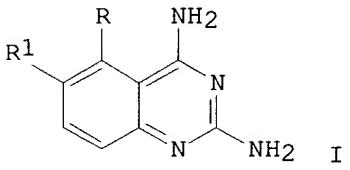
RN 50828-21-2 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-5-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)



RN 50930-12-6 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-5-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)


O
S
N
H2N
N
H

L44 ANSWER 61 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1981:417988 CAPLUS
DN 95:17988
TI Inhibition of dihydrofolate reductase: structure-activity correlations of quinazolines based upon molecular shape analysis
AU Battershell, Carol; Malhotra, D.; Hopfinger, A. J.
CS Case Inst. Technol., Case Western Reserve Univ., Cleveland, OH, 44106, USA
SO J. Med. Chem. (1981), 24(7), 812-18
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
GI



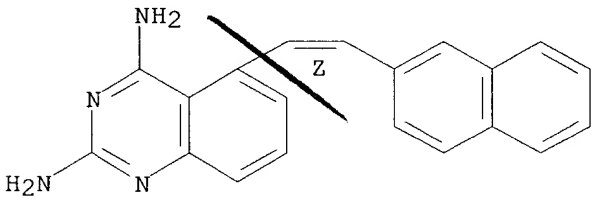
I

AB Quant. structure-activity anal. of 35 title compds. I (R and R1 = CN, Me, SC6H4CF3-m, etc.) as inhibitors of dihydrofolate reductase [9002-03-3] was carried out using mol. shape anal (MSA). Correlation equations were derived, one to explain the activities of I on the basis of their shape similarity to 2,4-diaminotriazine in its postulated active conformation (correlation coeff. of 0.965). Ability to quant. explain activity in a congeneric set of compds. using a structurally diverse ref. compd. indicates the potential to design new lead compds. using MSA.

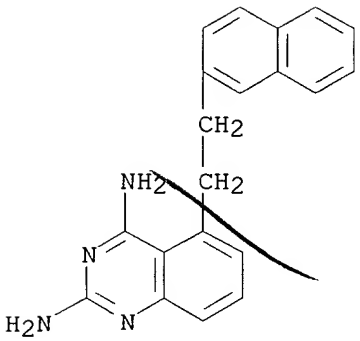
IT **50828-08-5 50828-09-6 50828-13-2**
50828-14-3 50828-17-6 50828-18-7
50828-20-1
RL: BIOL (Biological study)
(dihydrofolate reductase inhibition by, QSAR and mol. shape anal. in)

RN 50828-08-5 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethenyl]-, (Z)- (9CI) (CA INDEX NAME)

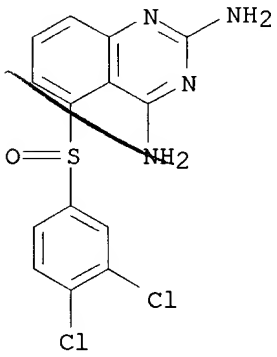
Double bond geometry as shown.



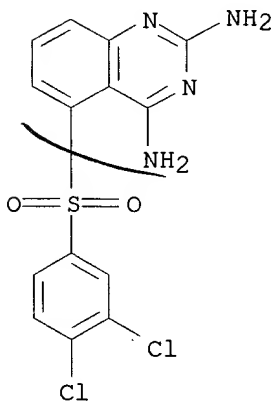
RN 50828-09-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethyl]- (9CI) (CA INDEX NAME)



RN 50828-13-2 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)sulfinyl]- (9CI) (CA INDEX NAME)



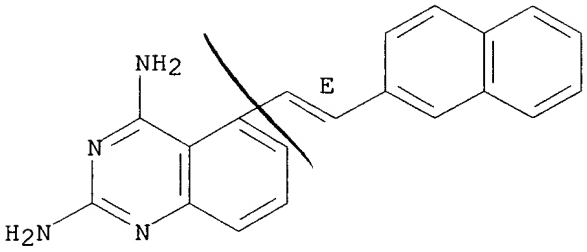
RN 50828-14-3 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



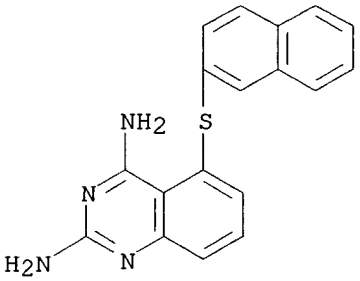
RN 50828-17-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethenyl]-, (E)- (9CI) (CA

INDEX NAME)

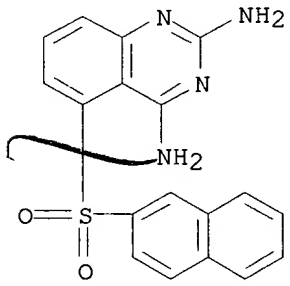
Double bond geometry as shown.



RN 50828-18-7 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

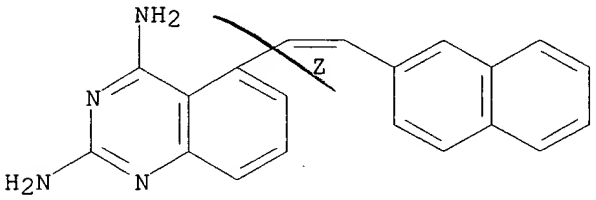


RN 50828-20-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)

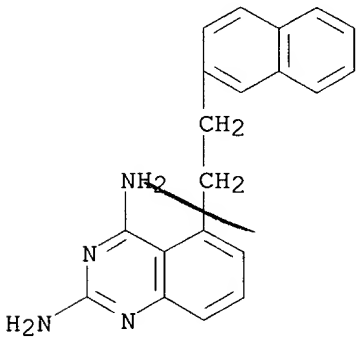


L14 ANSWER 62 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1980:418942 CAPLUS
DN 93:18942
TI Quantitative structure-activity relationships by distance geometry: systematic analysis of dihydrofolate reductase inhibitors
AU Crippen, Gordon M.
CS Dep. Chem., Texas A and M Univ., College Station, TX, 77843, USA
SO J. Med. Chem. (1980), 23(6), 599-606
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
AB Algorithms for the distance geometry approach to rationalizing ligand binding are presented for 68 quinazoline inhibitors of dihydrofolate reductase [9002-03-3] of Streptococcus faecium. Results are discussed and compared with the Hansch method of QSAR, and an improved inhibitor was predicted.
IT **50828-08-5 50828-09-6 50828-12-1**
50828-13-2 50828-14-3 50828-17-6
50828-18-7 50828-19-8 50828-20-1
50828-21-2 50930-12-6
RL: BIOL (Biological study)
(binding of, to dihydrofolate reductase, calcn. of free energy of)
RN 50828-08-5 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethenyl]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

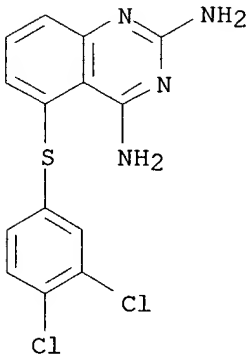


RN 50828-09-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethyl]- (9CI) (CA INDEX NAME)

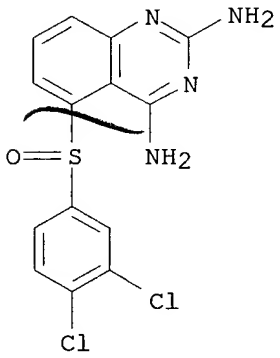


RN 50828-12-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)thio]- (9CI) (CA INDEX

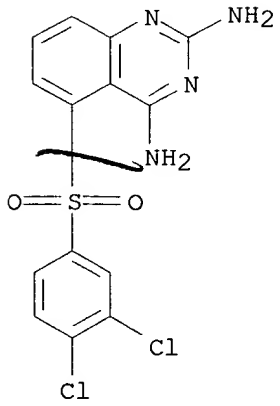
NAME)



RN 50828-13-2 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)sulfinyl]- (9CI) (CA INDEX NAME)

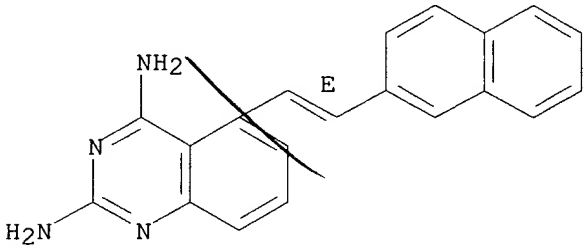


RN 50828-14-3 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

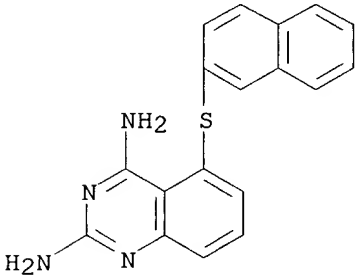


RN 50828-17-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

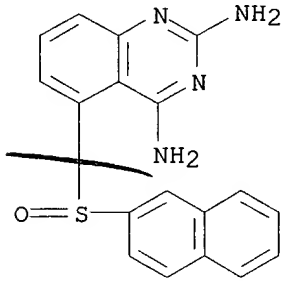
Double bond geometry as shown.



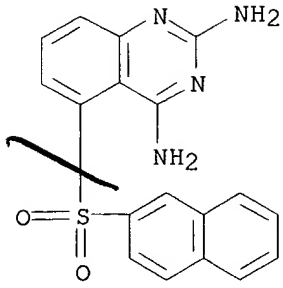
RN 50828-18-7 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)



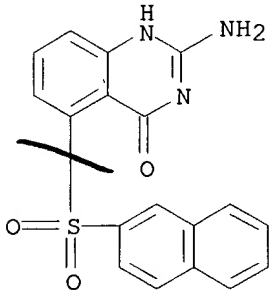
RN 50828-19-8 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylsulfinyl)- (9CI) (CA INDEX NAME)



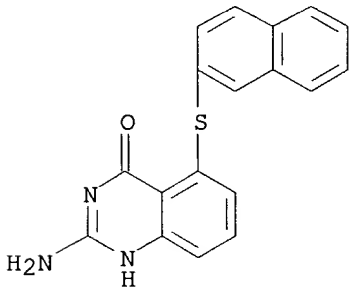
RN 50828-20-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)



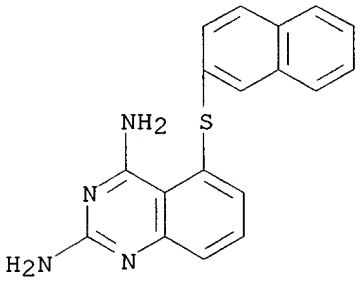
RN 50828-21-2 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-5-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)



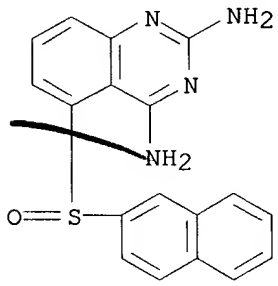
RN 50930-12-6 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-5-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)



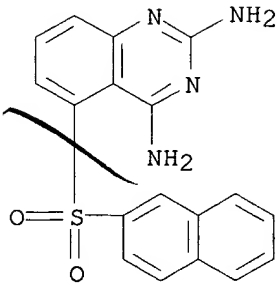
L1 ANSWER 63 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1979:468302 CAPLUS
DN 91:68302
TI Distance geometry approach to rationalizing binding data
AU Crippen, Gordon M.
CS Sch. Pharm., Univ. California, San Francisco, CA, 94143, USA
SO J. Med. Chem. (1979), 22(8), 988-97
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
AB A new method for calcg. quant. structure-activity relationships (QSAR) from data on binding affinity of ligands to a receptor site of proteins is presented. The binding data of 8 phenoxyacetone derivs. to .alpha.-chymotrypsin [9004-07-3] and of 22 quinazoline derivs. to dihydrofolate reductase [9002-03-3] is given.
IT **50828-18-7 50828-19-8 50828-20-1 50828-21-2 50930-12-6**
RL: PROC (Process)
(dihydrofolate reductase binding of, free energy in relation to)
RN 50828-18-7 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)



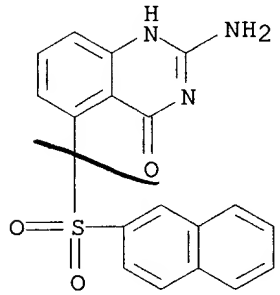
RN 50828-19-8 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylsulfinyl)- (9CI) (CA INDEX NAME)



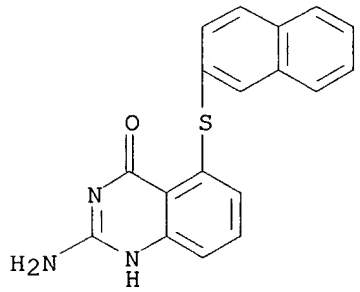
RN 50828-20-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)



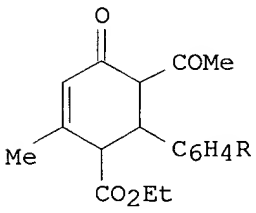
RN 50828-21-2 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-5-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)



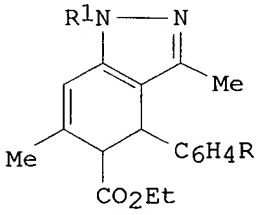
RN 50930-12-6 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-5-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)



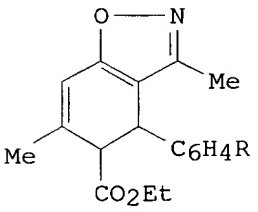
L14 ANSWER 64 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1978:120645 CAPLUS
DN 88:120645
TI Some reactions of 6-acetyl-5-aryl-4-carbethoxy-3-methylcyclohex-2-enones
AU Elkasaby, M. A.
CS Fac. Sci., Ain Shams Univ., Abbassia, Egypt
SO Indian J. Chem., Sect. B (1977), 15(8), 690-3
CODEN: IJSBDB; ISSN: 0376-4699
DT Journal
LA English
GI



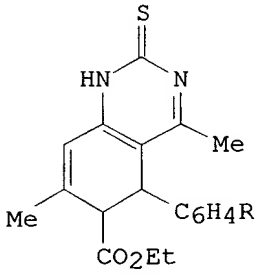
I



II



III

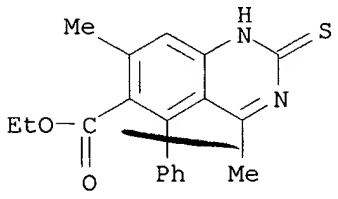


IV

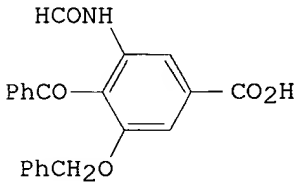
AB Title compds. I (R = H, OMe, NMe2, NO2, OH) were treated with R1NHNH2 (R1 = H, Ph, PhSO2, CONH2), HONH2 and thiourea to give dihydroindazoles II, dihydrobenzisoxazoles III and dihydroquinazoline-2(1H)-thiones IV, resp. Cyclocondensation of PhCH:C(COMe)CO2Et and its ring-substituted derivs. with MeCOCH2COMe gave I.

IT **65735-95-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 65735-95-7 CAPLUS
CN 6-Quinazolinecarboxylic acid, 1,2-dihydro-4,7-dimethyl-5-phenyl-2-thioxo-, ethyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 65 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1977:577454 CAPLUS
DN 87:177454
TI Aminobenzoic acid diuretics. 9. 3,4-Disubstituted 5-acylaminobenzoic acids and related compounds
AU Feit, Peter W.; Nielsen, Ole B. Tvaermose
CS Leo Pharm. Prod., Ballerup, Den.
SO J. Med. Chem. (1977), 20(12), 1687-91
CODEN: JMCMAR
DT Journal
LA English
GI

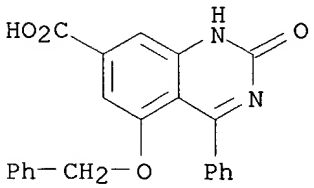


I

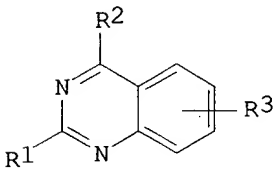
AB A series of 37 title acylamino-, alkylamino-, and ureidobenzoic acid derivs. and cyclic analogs were prepd. from the appropriate aminobenzoic acid derivs. by acylation or reaction with KOCN or an alkyl isocyanate. Several acetamido and formamido derivs. had diuretic potency in tests in dogs, with 4-benzoyl-3-benzyloxy-5-formamidobenzoic acid (I) [55232-85-4] having approx. 10% the potency of bumetanide. Structure-activity relations and diuretic action in relation to sulfamoyl analogs are discussed.

IT **64187-07-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as diuretic)

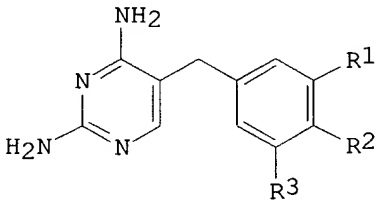
RN 64187-07-1 CAPLUS
CN 7-Quinazolinecarboxylic acid, 2,3-dihydro-2-oxo-4-phenyl-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



L14 ANSWER 66 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1977:25854 CAPLUS
DN 86:25854
TI Quantitative structure-activity relation of antimalarial and dihydrofolate reductase inhibition by quinazolines and 5-substituted benzyl-2,4-diaminopyrimidines
AU Hansch, Corwin; Fukunaga, James Y.; Jow, Priscilla Y. C.; Hynes, John B.
CS Dep. Chem., Pomona Coll., Claremont, Calif., USA
SO J. Med. Chem. (1977), 20(1), 96-102
CODEN: JMCMAR
DT Journal
LA English
GI



I



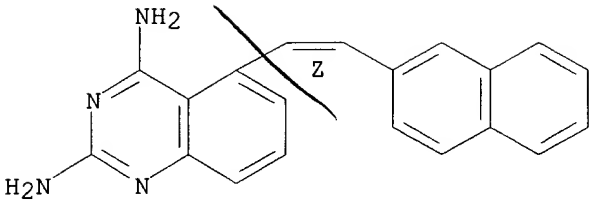
II

AB A quant. structure-activity relationship (QSAR) for the inhibition of dihydrofolate reductase [9002-03-3] from Streptococcus faecium by 68 quinazolines (I: R1, R2 = NH2, SH, OH; R3 = arylsulfonyl, arylthio, aralkylamino) was formulated. This was compared with a QSAR for inhibition of Escherichia coli dihydrofolate reductase by 10 2,4-diamino-5-benzylpyrimidines (II: R1 = H, OMe; R2 = H, Me, Cl, OH, OMe; R3 = H, Cl, OMe). The QSAR for inhibition of bacterial enzyme was compared with the QSAR for mammalian enzyme inhibition. A QSAR was also formulated for the antimalarial action of 64 quinazolines (I: R1 = R2 = NH2, BuNH, Me2N; R3 = aralkylamino, aralkyloxy, aryloxy, pyridyl, pyrrolyl, thienyl) and 6- and 8-aza analogs against Plasmodium berghei in mice. The antimalarial QSAR is consistent with the in vitro bacterial study.

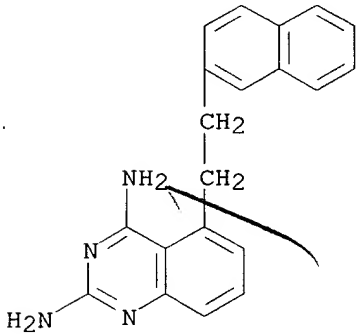
IT **50828-08-5 50828-09-6 50828-12-1**
50828-13-2 50828-14-3 50828-17-6
50828-18-7 50828-19-8 50828-20-1
50828-21-2 50930-12-6
RL: BIOL (Biological study)
(dihydrofolate reductase inhibition by, calcn. in relation to)

RN 50828-08-5 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethenyl]-, (Z)- (9CI) (CA INDEX NAME)

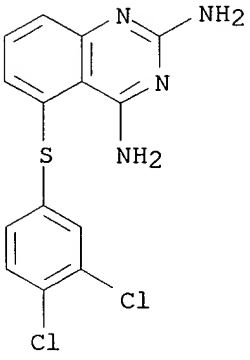
Double bond geometry as shown.



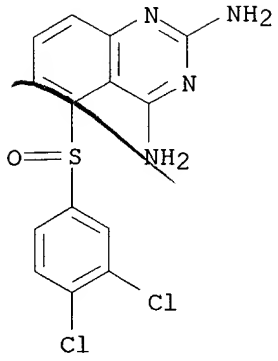
RN 50828-09-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethyl]- (9CI) (CA INDEX NAME)



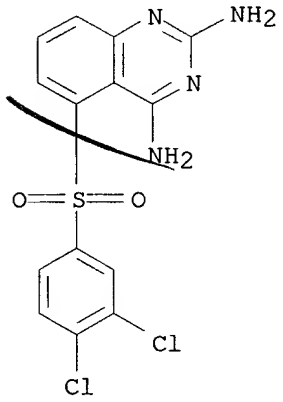
RN 50828-12-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)thio]- (9CI) (CA INDEX NAME)



RN 50828-13-2 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)sulfinyl]- (9CI) (CA INDEX NAME)

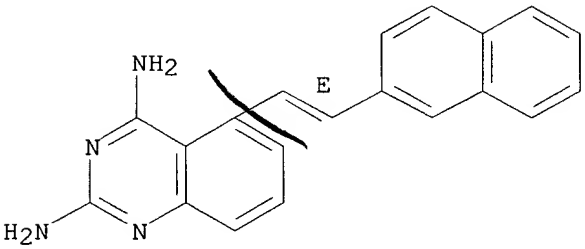


RN 50828-14-3 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

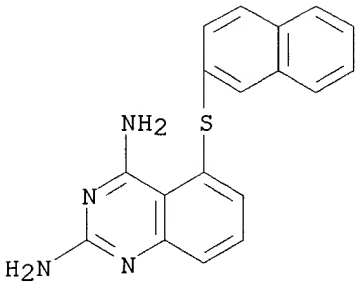


RN 50828-17-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

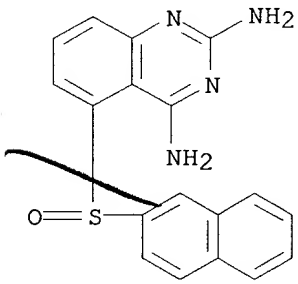
Double bond geometry as shown.



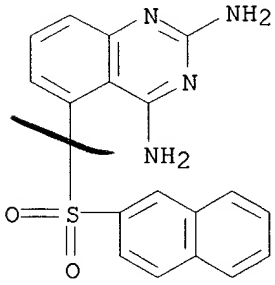
RN 50828-18-7 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)



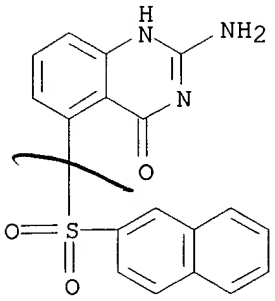
RN 50828-19-8 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylsulfinyl)- (9CI) (CA INDEX NAME)



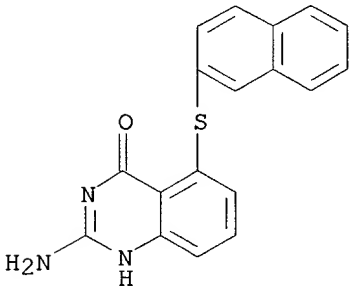
RN 50828-20-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)



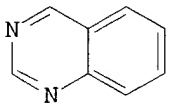
RN 50828-21-2 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-5-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)



RN 50930-12-6 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-5-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)



L14 ANSWER 67 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1976:144572 CAPLUS
DN 84:144572
TI Inhibition of dihydrofolate reductase. Structure-activity correlations of quinazolines
AU Fukunaga, James Y.; Hansch, Corwin; Steller, Edward E.
CS Dep. Chem., Pomona Coll., Claremont, Calif., USA
SO J. Med. Chem. (1976), 19(5), 605-11
CODEN: JMCMAR
DT Journal
LA English
GI



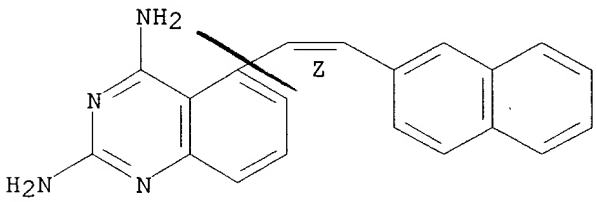
I

AB A quant. structure-activity relationship(QSAR) was formulated for about 100 derivs. of quinazoline (I) [253-82-7] causing 50% inhibition of liver dihydrofolate reductase [9002-03-3]. The QSAR for the quinazolines was compared to those for inhibitors consisting of derivs. of s-triazine [290-87-9] and pyrimidine [289-95-2]. The application of equations from the 3 QSAR studies to the design of new inhibitors of dihydrofolate reductase was discussed.

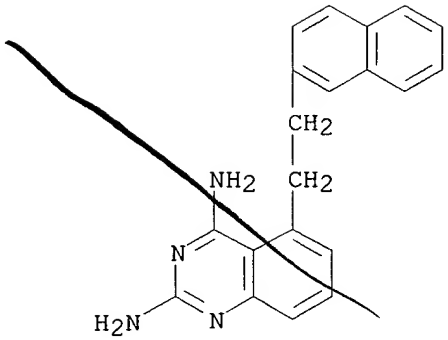
IT **50828-08-5 50828-09-6 50828-12-1**
50828-13-2 50828-14-3 50828-17-6
50828-18-7 50828-19-8 50828-20-1
50828-21-2 50930-12-6
RL: BIOL (Biological study)
(dihydrofolate reductase inhibition by, calcn. of)

RN 50828-08-5 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethenyl]-, (Z)- (9CI) (CA INDEX NAME)

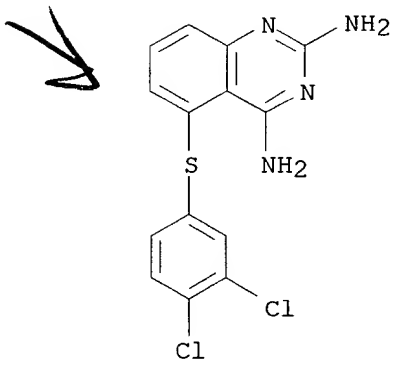
Double bond geometry as shown.



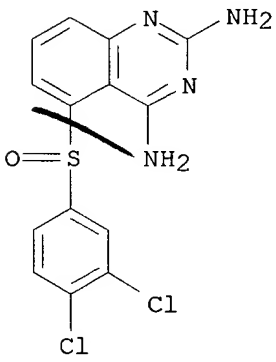
RN 50828-09-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethyl]- (9CI) (CA INDEX NAME)



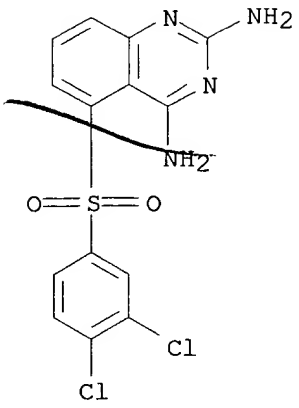
RN 50828-12-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)thio]- (9CI) (CA INDEX NAME)



RN 50828-13-2 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)sulfinyl]- (9CI) (CA INDEX NAME)

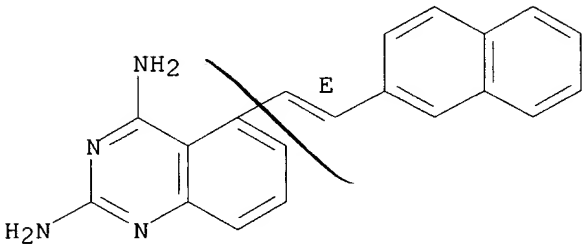


RN 50828-14-3 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

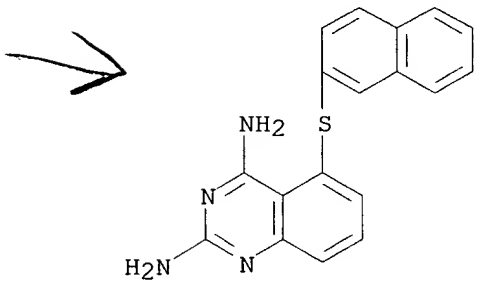


RN 50828-17-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

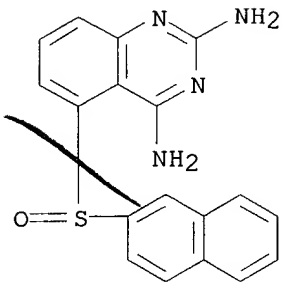
Double bond geometry as shown.



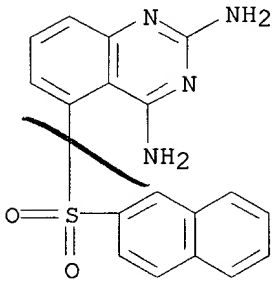
RN 50828-18-7 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)



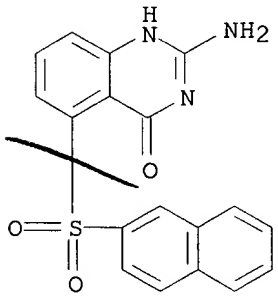
RN 50828-19-8 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylsulfinyl)- (9CI) (CA INDEX NAME)



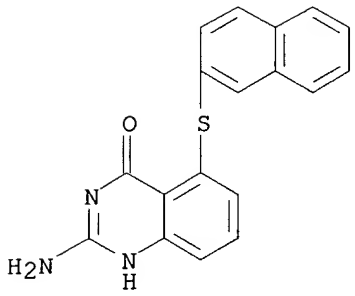
RN 50828-20-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)



RN 50828-21-2 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-5-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)



RN 50930-12-6 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-5-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)


O
S
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H_2N
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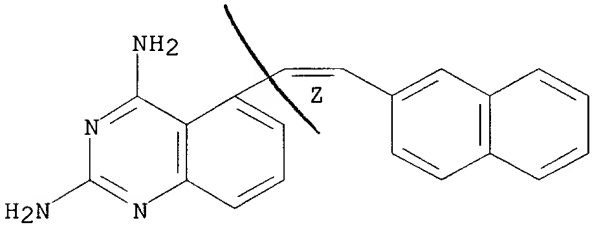
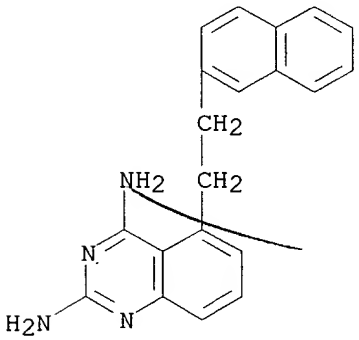
L14 ANSWER 68 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1975:25675 CAPLUS
DN 82:25675
TI Quinazolines as inhibitors of dihydrofolate reductase. 2
AU Hynes, John B.; Ashton, Wallace T.; Bryansmith, Dale; Freisheim, James H.
CS Coll. Pharm., Med. Univ. South Carolina, Charleston, S. C., USA
SO J. Med. Chem. (1974), 17(9), 1023-5
CODEN: JMCMAR
DT Journal
LA English
GI For diagram(s), see printed CA Issue.
AB Of 37 5- and 6-arylthioquinazolines tested, 2,4-diamino-6-(2-naphthylsulfonyl)quinazoline [51123-83-2] was the most active inhibitor of dihydrofolate reductase [9002-03-3] from rat liver or from Streptococcus faecium, with an I50 of 0.004 .mu.M in each case. Structure-activity relations were discussed.
IT **50828-08-5 50828-09-6 50828-12-1**
50828-13-2 50828-14-3 50828-15-4
50828-17-6 50828-18-7 50828-19-8
50828-20-1 50828-21-2 50930-12-6
RL: BIOL (Biological study)
(dihydrofolate reductase inhibition by)
RN 50828-08-5 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethenyl]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

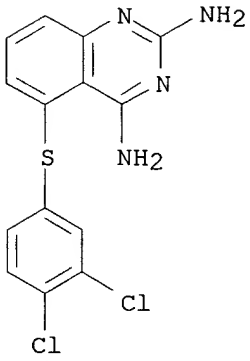


RN 50828-09-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethyl]- (9CI) (CA INDEX NAME)

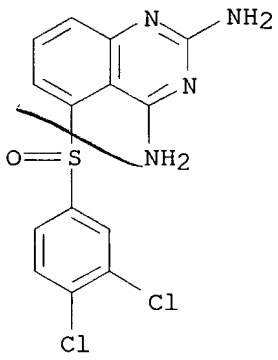


RN 50828-12-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)thio]- (9CI) (CA INDEX

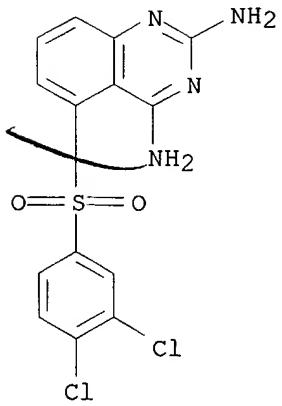
NAME)



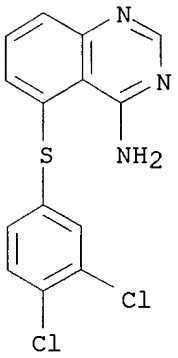
RN 50828-13-2 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)sulfinyl]- (9CI) (CA INDEX NAME)



RN 50828-14-3 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

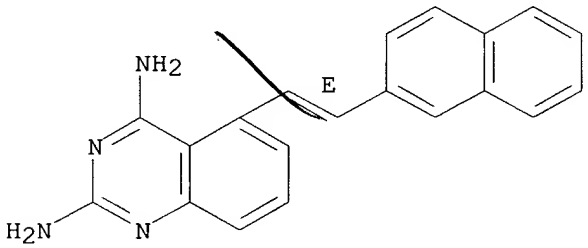


RN 50828-15-4 CAPLUS
CN 4-Quinazolinamine, 5-[(3,4-dichlorophenyl)thio]- (9CI) (CA INDEX NAME)

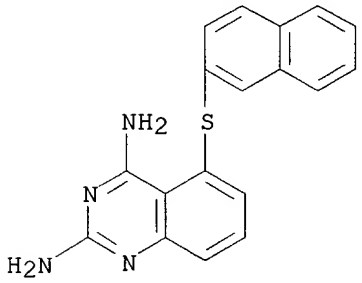


RN 50828-17-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

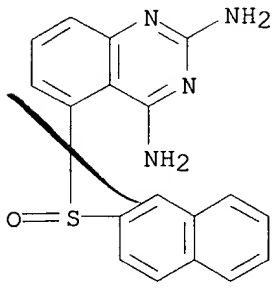
Double bond geometry as shown.



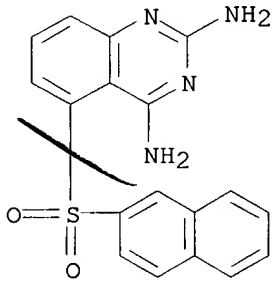
RN 50828-18-7 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)



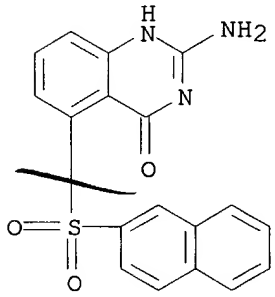
RN 50828-19-8 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylsulfinyl)- (9CI) (CA INDEX NAME)



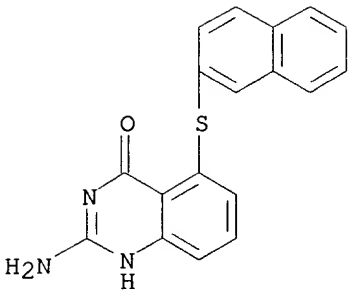
RN 50828-20-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)



RN 50828-21-2 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-5-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)



RN 50930-12-6 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-5-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)


O
S
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H_2N
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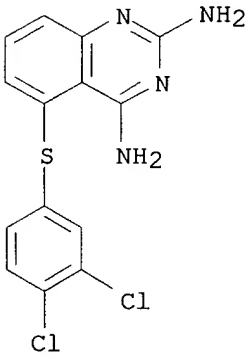
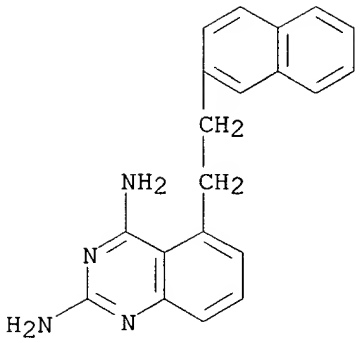
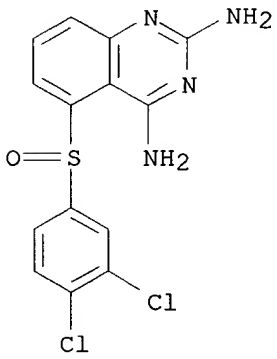
L14 ANSWER 69 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1973:542797 CAPLUS
DN 79:142797
TI Synthesis of 5-substituted quinazolines as potential antimalarial agents
AU Ashton, Wallace T.; Hynes, John B.
CS Coll. Pharm., Med. Univ. South Carolina, Charleston, S. C., USA
SO J. Med. Chem. (1973), 16(11), 1233-7
CODEN: JMCMAR
DT Journal
LA English
AB None of a series of 5-arylmethyl-, 5-arylthio-, and 5-arylthiomethyl-2,4-diaminoquinazolines and related compds. showed activity against Plasmodium berghei in mice even at 640 mg/kg. However, several compds. were highly potent inhibitors of rat liver dihydrofolate reductase [9002-03-3] in vitro, e.g. 2,4-diamino-5-(2-naphthylthiomethyl)quinazoline (I) [43170-98-5] at 0.01 .mu.M. Evidently, quinazolines bearing a bulky group at position 5 may not effectively cross the plasmodial membrane. I was prepd. by converting 2-methyl-6-nitroaniline [570-24-1] by diazotization and CuCl-KCN to the benzonitrile, monobrominating the Me photochem. with 1,3-dibromo-5,5-dimethylhydantoin, using the product to alkylate 2-naphthalenethiol [91-60-1], reducing the NO2 to NH2 with SnCl2, and cyclizing with chloroformanidine-HCl [29671-92-9].
IT **50828-12-1**
RL: RCT (Reactant)
(oxidn. of)
RN 50828-12-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)thio]- (9CI) (CA INDEX NAME)



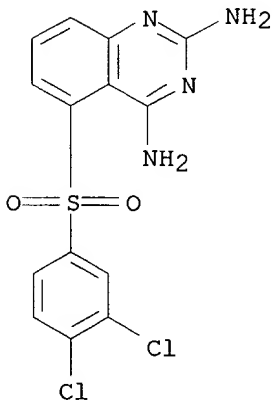
IT **50828-09-6P 50828-13-2P 50828-14-3P**
50828-15-4P 50828-17-6P 50828-18-7P
50828-19-8P 50828-20-1P 50828-21-2P
50930-12-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 50828-09-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethyl]- (9CI) (CA INDEX NAME)



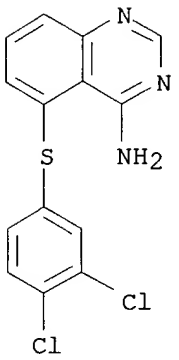
RN 50828-13-2 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)sulfinyl]- (9CI) (CA INDEX NAME)



RN 50828-14-3 CAPLUS
CN 2,4-Quinazolinediamine, 5-[(3,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

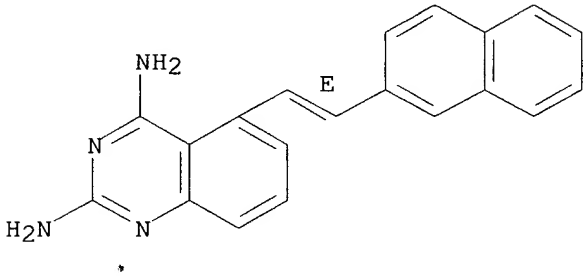


RN 50828-15-4 CAPLUS
CN 4-Quinazolinamine, 5-[(3,4-dichlorophenyl)thio]- (9CI) (CA INDEX NAME)

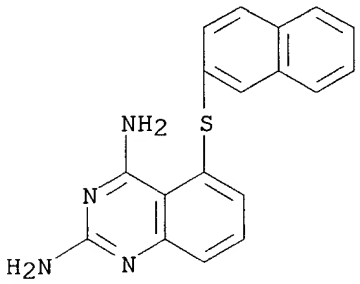


RN 50828-17-6 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

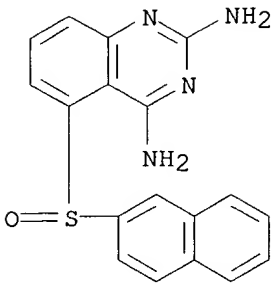
Double bond geometry as shown.



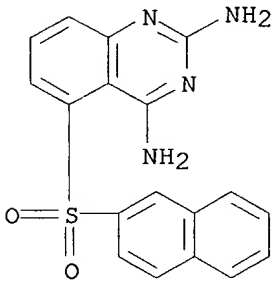
RN 50828-18-7 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)



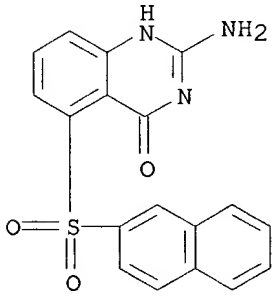
RN 50828-19-8 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylsulfinyl)- (9CI) (CA INDEX NAME)



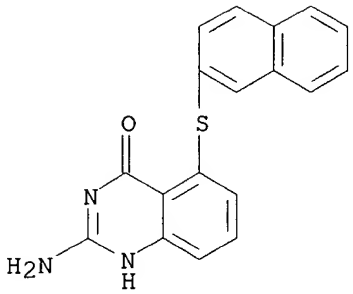
RN 50828-20-1 CAPLUS
CN 2,4-Quinazolinediamine, 5-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)



RN 50828-21-2 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-5-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)

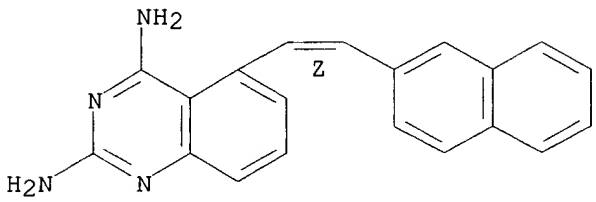


RN 50930-12-6 CAPLUS
CN 4(1H)-Quinazolinone, 2-amino-5-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)



IT **50828-08-5**
RL: RCT (Reactant)
(redn. of)
RN 50828-08-5 CAPLUS
CN 2,4-Quinazolinediamine, 5-[2-(2-naphthalenyl)ethenyl]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



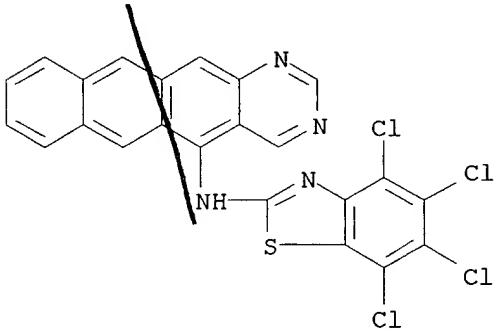
L14 ANSWER 70 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1972:516041 CAPLUS
DN 77:116041
TI Anthraquinone pigment dyes
IN Wessling, Diether; Leister, Heinrich; Degener, Eberhart
PA Farbenfabriken Bayer A.-G.
SO Ger. Offen., 80 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2059724	A	19720608	DE 1970-2059724	19701204
	IT 945217	A	19730510	IT 1971-54450	19711201
	GB 1345635	A	19740130	GB 1971-56021	19711202
	BE 776208	A1	19720605	BE 1971-111243	19711203
	NL 7116668	A	19720606	NL 1971-16668	19711203
	FR 2116549	A5	19720713	FR 1971-43609	19711203
	FR 2116549	B1	19750829		
	US 3899504	A	19750812	US 1971-204722	19711203
PRAI	DE 1970-2059724		19701204		
	DE 1970-2064911		19701204		

AB Ten anthraquinones, a dianthrimide, and an anthrapyrimidine contg. one or two tetrahalobenzothiazolylamino groups (QNH, X = Cl or Br) in the aromatic ring were prepd. by reaction of QCl with the appropriate amino compd. The compds. are liight- and migrationfast pigments for coatings, plastics, and textiles. For example, 1,5-diaminoanthraquinone and QCl(X = Cl) were added to fused PhOH at 80-100.deg., and the mixt. was heated 1 hr at 160.deg. and 8 hr at 180.deg. to give a red pigment (I, X = Cl in Q) [36411-98-0].

IT **38151-83-6P**
RL: IMF (Industrial manufacture); PREP (Preparation)
(prepn. of)

RN 38151-83-6 CAPLUS
CN Naphtho[2,3-g]quinazolin-5-amine, N-(4,5,6,7-tetrachloro-2-benzothiazolyl)- (9CI) (CA INDEX NAME)



L14 ANSWER 71 OF 71 CAPLUS COPYRIGHT 2002 ACS
AN 1968:39584 CAPLUS
DN 68:39584
TI Synthesis and biological activity of some 5,6-dihydroquinazolines
AU Smith, Walter Thomas, Jr.; Sellas, James T.
CS State Univ. of Iowa, Iowa City, Iowa, USA
SO Chim. Ther. (1967), 2(2), 148-50
CODEN: CHTQAC
DT Journal
LA English
GI For diagram(s), see printed CA Issue.
AB A mixt. of 51.7 g. acetylacetone, 37.25 g. p-Me2NC6H4CHO, 8 ml. piperidine, and 10 ml. 95% EtOH was heated slightly to give a clear soln. and kept at room temp. for 1-3 days. The solid was dissolved in 11.95% EtOH, cooled, and filtered to give I (R = NMe2), m. 181.degree.. Similarly prepd. were I (R = NO2), m. 174-5.degree., I (R = Cl), m. 169.degree., I (R = OH), m. 153.degree., and I (R = OH).bul.MeOH, m. 158.degree.. A mixt. of 10 g. I (R = H) and 24 g. guanidine carbonate was heated 2 hrs. at 190.degree. in a water bath, cooled, taken up in 200 ml. dil. HCl, and filtered. The filtrate was cooled, made alk. with cold dil. NH4OH, filtered, and dried. The ppt. was extd. with 200 ml. dry C6H6 in a Soxhlet extractor and concd. to 75 ml. to give 1 g. II (R = H), m. 228-30.degree.. Similarly prepd. were II (R = OH), m. 244.degree. (decompn.), II (R = OMe), m. 181.degree., and II (R = Cl), m. 191-2.degree.. A mixt. of 1 g. II (R = H) and 1 g. 10% Pd-C in 30 ml. mesitylene was refluxed 24 hrs. under CO2 and filtered and the filtrate was extd. with dil. HCl. The acid exts. were cooled and made alk. with NH4OH to give 0.5 g. 2-amino-4,7-dimethyl-5-phenylquinazoline, m. 210-11.degree. (abs. EtOH). As a carbonic anhydrase inhibitor, a 170 .times. 10-7M soln. of II (R = H) was equiv. to a 0.1 .times. 10-7 soln. of Diamox. II (R = OMe) showed slight activity as a coronary dilator.
IT **16873-85-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 16873-85-1 CAPLUS
CN Quinazoline, 2-amino-4,7-dimethyl-5-phenyl- (8CI) (CA INDEX NAME)